



INDIAN AGRICULTURAL
RESEARCH INSTITUTE, NEW DELHI.

I A. R. I. 6.

S. C. P-1/8/47-P. J.-17.5-48 2000

MICROBIOLOGY AND PATHOLOGY

MICROBIOLOGY AND PATHOLOGY

BY

CHARLES F. CARTER, B.S., M.D.

Instructor in Pathology and Applied Microbiology, Parkland Hospital School of Nursing, Dallas, Texas; Director, Carter's Clinical Laboratory, Dallas, Texas; Consulting Pathologist, St. Louis Southwestern Railway Hospital, Texarkana, Arkansas; Consulting Pathologist, Mother Frances Hospital, Tyler, Texas; Formerly Director of Laboratories, Parkland Hospital

WITH 216 TEXT ILLUSTRATIONS AND
25 COLOR PLATES

FOURTH EDITION

ST. LOUIS
THE C. V. MOSBY COMPANY
1948

COPYRIGHT, 1936, 1939, 1944, 1948, BY THE C. V. MOSBY COMPANY

(All rights reserved)

Reprinted October, 1948

Printed in the
United States of America

*Press of
The C. V. Mosby Company
St. Louis*

TO

MY WIFE

ANN

MY CHILDREN

BILL AND TRUMAN

AND

MY SISTER

BLYNN

THIS VOLUME IS AFFECTIONATELY
DEDICATED

PREFACE TO FOURTH EDITION

Since the appearance of the last edition of this book the sciences of both microbiology and pathology have undergone great progress. In the field of microbiology, development has been truly phenomenal because it was during this time that the sulfonamide compounds reached their present state of effectiveness and the antibiotic drugs came into practical use. So rapid has been this development that methods which only a few years ago were new are now obsolete. In revising the chapters on microbiology it has been the purpose of the author to omit the obsolete and include the new. This has necessitated a revision of all chapters and in the case of some chapters this revision has been very extensive. The treatment of microbial infections by means of the sulfonamide compounds and the antibiotics is discussed. A new chapter on Approved Methods of Immunization has been added.

In the section on pathology much of the material has been rearranged and rewritten. Infectious hepatitis and homologous serum jaundice are discussed. New chapters on The Hospital Pathologist and His Work and on Defects of Body Development have been included. Other chapters have undergone extensive revision.

I am grateful to Miss Laura L. Simms, B.A., R.N., Instructor in Nursing Arts, Baylor Hospital School of Nursing, for preparing the questions for many chapters, and to Mr. William F. Carter for suggestions in connection with the writing of the chapter on Defects of Body Development and for preparing the questions on that chapter. The typographical work was efficiently done by Miss Helen Petteway. Miss Lilly Jane Jones and Miss Charlene Brown were of great assistance in the preparation of the index.

To Damon Bernwanger, Charlene Brown, Truman Carter, Shirley Clark, Ora Davis, Norman Jones, Vennie Louise Langford, Betty Lou Larsen, Helen Petteway, I express my thanks for their help in preparing illustrations and to Mr. A. B. Gary for his photographic work.

CHARLES F. CARTER.

Dallas, Texas.

PREFACE TO THE FIRST EDITION

The first part of this book, which deals with microbiology, is an outgrowth of *Bacteriology for Nurses* written by me in 1928 and published by The C. V. Mosby Co. The fact that the previous publication found a place in schools of nursing that exceeded the expectation of both myself and the publishers has given courage to the present undertaking. The second part of the book, which deals with pathology and is entirely new, is added because both I and the publishers believe that such a combined publication is particularly well fitted to meet the requirements of the curriculum of the modern school of nursing. Throughout the book, I have attempted to follow as closely as possible the outline prepared by the Committee on Education of the National League of Nursing Education as a part of their model curriculum. I have deviated therefrom only in those cases in which my experience as a teacher of nurses has indicated that such deviation gave greater clearness or increased the scope of knowledge.

Although the portion of the book dealing with microbiology is based on a previous work, the subject matter has been completely rewritten and rearranged. The scope of the book has been considerably broadened, and the text has been brought up to date. An effort has been made to present the fundamentals of microbiology in such a manner that the nurse will realize that microbes play an important part not only in disease, but also in the processes of nature, in agriculture, and in industry.

From the medical standpoint, how microbes get into the body, how the body resists them, why disease is sometimes produced and is not produced at other times, and how microbes are thrown off from the body, are especially stressed because it is upon these factors that the scientific nursing of infectious diseases and their prevention depend. The practical application of immunological methods, vaccine therapy, and serum therapy are emphasized and their scientific basis is explained.

Throughout the portion of the book devoted to pathology the idea that the signs and symptoms of disease are but outward manifestations of underlying changes is constantly kept before the mind of the nurse. How these changes are brought about and how the body reacts to them, causing the manifestations of disease, are explained, and practical application of this knowledge is made to bedside nursing. Although the fundamentals of pathology are primarily emphasized, a brief consideration of the facts of special pathology is included. In order that the text may be better understood, short laboratory exercises are appended to those chapters in which such exercises are thought to be of value.

I want it to be understood that this work is not entirely my own, because if it had not been for the help of Miss Emma Pope, Educational Director of Parkland Hospital School of Nursing, this book in its present form would not have appeared. She has read the manuscript, made numerous suggestions, and prepared many of the questions. In addition, many of the teaching ideas incorporated in the text are hers. My debt to her I fully acknowledge.

I am deeply grateful to Miss Kathryn Pettaway and Miss Hattie Lee Pemberton, both of whom have freely given their time in preparing illustrations and reading the manuscript. The manuscript in its final form was prepared by Miss Ruth Ragsdale.

The text has greatly profited by being permitted to use various illustrations from the works of other authors and from the catalogues of dealers in scientific supplies. In each case full credit has been given, but, in addition, thanks are here expressed to the different authors, publishers, and commercial organizations whose generosity made this possible.

CHARLES F. CARTER.

Dallas, Texas.

CONTENTS

PART I MICROBIOLOGY

SECTION I GENERAL PRINCIPLES OF MICROBIOLOGY

CHAPTER I	PAGE
HISTORY OF MICROBIOLOGY—ITS VALUE - - - - -	29
The Value of a Knowledge of Microbiology, 39; True-False Test, 40; Completion Test, 40.	
CHAPTER II	
RELATION OF MICROBES TO OTHER LIVING THINGS—RELATION OF MICROBIOLOGY TO OTHER SCIENCES - - - - -	42
Principles of Biological Classification, 43; Relation of Bacteria to Other Plants, 44; Lower Forms of Animal Life, 44; Questions for Review, 45.	
CHAPTER III	
THE EQUIPMENT OF THE MICROBIOLOGIST - - - - -	46
The Microscope, 46; General Description, 46; Care and Use of the Microscope, 49; The Electron Microscope, 52; The Photomicrographic Camera, 54; The Bacteriological Incubator, 54; Constant Temperature Water Bath, 55; Centrifuge, 57; Sterilizing Equipment, 57; Refrigerator, 58; Other Essential Equipment, 58.	
CHAPTER IV	
THE CELL - - - - -	59
Protoplasm, 59; Size and Shape of Cells, 59; Structure of Cells, 60; All Typical Structure Not Present in Every Cell, 61; Definition of Cell, 61; Multiplication of Cells, 62; Unicellular Organisms: Nutrition, Circulation, Respiration, Excretion, and Response to Stimuli, 63; Locomotion of Unicellular Organisms, 63; Reproduction of Unicellular Organisms, 64; True-False Test, 64; Completion Test, 64.	
CHAPTER V	
GENERAL CHARACTERISTICS OF BACTERIA - - - - -	66
Definition, 66; Distribution and Importance, 66; Chemical Composition of Bacteria, 66; Shape and Arrangement of Bac-	

teria, 67; Size of Bacteria, 68; Structure of Bacteria, 69; Motility, 70; Reproduction, 71; Spore Formation, 71; Classification of Bacteria, 73; Bacterial Variation, 74; Adaptability of Bacteria, 76; Drug Fastness, 77; True-False Test, 77; Completion Test, 78.

CHAPTER VI

CONDITIONS AFFECTING THE GROWTH OF BACTERIA - - - - -	79
Food, 79; Moisture, 80; Temperature, 80; Reaction, 82; Oxygen, 82; Light, 82; Products of Bacterial Growth, 83; Electricity, 83; Chemicals, 83; Osmosis, 83; Shaking, 84; Pressure, 84; Symbiosis and Antagonism, 84; True-False Test, 85; Completion Test, 86.	

CHAPTER VII

SPECIAL ACTIVITIES OF BACTERIA - - - - -	87
Production of Enzymes; Putrefaction; Fermentation, 87; Ptomaines, 89; Nitrification, Nitrogen Fixation, and Denitrification, 90; Toxins, 90; Hemolysins, Leucocidins, Coagulase, and Fibrinolysin, 92; Spreading Factor, 93; Pigment Production, 93; Heat Production, 93; Light Production, 93; Odors, 93; True-False Test, 94; Completion Test, 94.	

CHAPTER VIII

METHODS OF STUDYING BACTERIA - - - - -	96
Examination of Unstained Bacteria-Staining Methods, 96; Examination of Unstained Bacteria, 96; Hanging-Drop Preparations, 96; Dark-Field Illumination, 98; Fixing and Staining Methods, 99; General Stains, 100; Differential Stains, 101; Gram's Method of Staining, 101; Staining for Acid-Fastness, 103; Stains for Specific Organisms, 105; Stains for Certain Parts of Bacteria, 105; Questions for Review, 105; True-False Test, 105; Completion Test, 106.	

CHAPTER IX

THE STUDY OF BACTERIA BY CULTURAL METHODS AND ANIMAL INOCULATION - - - - -	107
Culture Media, 107; Selective and Differential Media, 110; Sulfonamide and Penicillin Inhibiting Media, 111; Making Cultures, 112; Pure Cultures, 113; Streak Plates, 117; How Pure Cultures Are Studied, 118; Determination of Fermentation Reactions of Bacteria on Carbohydrates, 118; Counting Bacteria by Plating, 118; Culturing Anaerobic Bacteria, 120; Animal Inoculation, 121; Questions for Review, 124; True-False Test, 124; Completion Test, 125.	

CHAPTER X		PAGE
COLLECTION OF SPECIMENS FOR BACTERIOLOGICAL EXAMINATION -		126
Urine, 128; Blood for Cultures, 128; Blood for Serological Examinations, 130; Blood for the Estimation of the Sulfonamide Compounds, 130; Blood for the Estimation of Penicillin, 130; Sputum, 130; Cultures From the Nose and Throat, 131; Feces, 132; Pus, 132; Smears for Gonococci, 132; Cerebrospinal Fluid, 133; Pleural and Peritoneal Fluids, 133; Smears and Cultures From the Conjunctiva, 133; Questions for Review, 134.		
CHAPTER XI		
REMOVAL OR DESTRUCTION OF BACTERIA BY MECHANICAL AND PHYSICAL MEANS - - - - -		135
Removal or Destruction of Bacteria by Mechanical Means, 135; Sterilization by Physical Means, 136; Natural Methods of Removing or Destroying Bacteria, 142; Questions for Review, 143; Completion Test, 143.		
CHAPTER XII		
THE DESTRUCTION OF BACTERIA BY CHEMICALS - - - - -		144
How Disinfectants Act, 144; Qualities of a Good Disinfectant, 145; Factors Influencing the Action of Disinfectants, 145; Standardization of Disinfectants and Antiseptics, 146; Common Disinfectants and Antiseptics, 147; Soap, 147; Bichloride of Mercury, 147; Mercuric Iodide, 148; Mercurochrome, 148; Metaphen, 148; Merthiolate, 148; Mercresin, 148; Alcohol, 149; Boric Acid, 149; Fuming Nitric Acid, 149; Hydrogen Peroxide, 149; Sodium Perborate, 149; Silver Nitrate, 149; Protargol and Neosilvol, 149; Copper Sulphate, 149; Ferrous Sulphate, 150; Potassium Permanganate, 150; Lime, 150; Chlorine, 151; Tincture of Iodine, 152; Phenol, 152; Tricresol, 152; Sulphur Dioxide, 152; Formaldehyde, 152; Chlorothymol, 153; Dyes, 153; Treatment of Microbial Diseases With Chemicals, 153; Tyrothricin, 155; Penicillin, 155; Streptomycin, 155; Questions for Review, 155; True-False Test, 156; Completion Test, 156.		
CHAPTER XIII		
PRACTICAL DISINFECTION AND STERILIZATION - - - - -		158
Surgical Disinfection, 158; Instruments, 158; Hypodermic Syringes and Needles, 158; Dressings, Linens, Etc., 159; Gloves, 159; Hand Brushes, 160; Sutures and Ligatures, 160; Water and Salt Solution, 160; Hard Rubber Goods, 160; Soft Rubber Catheters, 160; Silk Catheters and Bougies, 160; Rubber Tubing for Intravenous Medication, 160; Cystoscopes, 161; Hands, 161; Site of Operation, 163; Oper-		

PAGE

ating Room, 163; Mucous Membranes, 164; Wound Disinfection, 164; Disinfection of Excreta and Contaminated Materials From Infectious Diseases, 164; The Hands of the Nurse, 165; Soiled Clothing, Bed Linen, Etc., 165; Shoes, 166; Feces and Urine, 166; Discharges From the Mouth and Nose, 167; Sputum, 167; Clinical Thermometers, 167; Eating Utensils, 167; Terminal Disinfection, 168; Disinfection of Articles for Public Use, 168; Water Closets, 168; The Woodwork of Schoolhouses, Churches, Theaters, 168; Public Conveyances, 168; Fumigation of Rooms and Disinfection of Air, 168; Fumigation, 168; Air Disinfection, 169; Questions for Review, 169.

CHAPTER XIV

THE WORK OF USEFUL BACTERIA - - - - -	171
Bacteria in the Processes of Nature, 172; Commercial Uses of Bacteria, 174; Manufacture of Dairy Products, 174; Manufacture of Alcoholic Beverages, 175; Baking, 176; Manufacture of Vinegar, 176; Sauerkraut, 176; Tanning, 177; Curing of Tobacco, 177; Retting of Flax and Hemp, 177; Manufacture of Antibiotics, 177; Other Commercial Uses of Bacteria, 177; Questions for Review, 177; True-False Test, 178.	

SECTION II

RELATION OF BACTERIA TO DISEASE

CHAPTER XV

BACTERIA AND DISEASE - - - - -	179
Source of the Bacteria Causing Infections, 179; How Pathogenic Bacteria Reach the Body, 180; How Bacteria Enter the Body, 181; Factors Influencing the Occurrence of Infection, 182; How Bacteria Cause Disease, 183; Local Effects of Bacteria, 184; General Effects of Bacteria, 184; Incubation Period, 184; Types of Infection Produced by Bacteria, 185; How Bacteria Are Thrown Off From the Body, 186; Koch's Postulates, 186; Questions for Review, 187; True-False Test, 187; Completion Test, 187.	

CHAPTER XVI

DEFENSES OF THE BODY AGAINST INFECTION. IMMUNITY - - -	189
Immunity Defined, 189; Immunity-Producing Diseases, 190; The Two Theories of Immunity, 190; Immunity Due to Antibody Formation, 191; Ehrlich's Side-Chain Theory of Antibody Production, 192; Complement, 193; Antitoxins, 194;	

Bacteriolysins, 194; Agglutinins, 194; Precipitins, 198; Heterophile Antibodies, 198; Opsonins, 199; Virus-Neutralizing Antibodies, 200; Phagocytosis, 200; Kinds of Immunity, 202; The Relation Existing Between Exposure to Disease and Immunity, 204; Immunological Methods of Studying Bacteria and Diagnosing Disease, 205; The Principle of Complement Fixation, 205; Questions for Review, 209; True-False Test, 210; Completion Test, 210.

CHAPTER XVII

VACCINES AND IMMUNE SERUMS - - - - -	212
Antitoxins, 213; Antivenins (Snake Poison Antitoxins), 214; Antibacterial Serums, 215; Convalescent Serum Therapy, 215; How Vaccines Are Prepared, 216; Questions for Review, 220; True-False Test, 220; Completion Test, 221.	

CHAPTER XVIII

HYPERSENSITIVENESS - - - - -	222
Anaphylaxis, 223; Allergy, 225; Bacterial Allergy, 229; Urticaria and Allergic Skin Eruptions, 229; Sensitivity to Drugs, 229; Hypersensitiveness to Vaccines, 229; Laboratory Tests to Detect Hypersensitiveness, 230; Desensitization, 230; True-False Test, 231; Completion Test, 231.	

CHAPTER XIX

HOW COMMUNICABLE DISEASES ARE TRANSMITTED - - - - -	233
Direct Contact, 233; Indirect Contact, 233; Insects, 234; Human Carriers, 235; Animals, 236; Fomites, 237; Food, 237; Questions for Review, 237; True-False Test, 237; Completion Test, 238.	

SECTION III

BACTERIOLOGY OF WATER AND MILK

CHAPTER XX

WATER, SWIMMING POOLS, SEWAGE - - - - -	239
Diseases Spread by Water, 239; Sources of Water, 240; Bacteriological Examination of Water, 240; Drinking Water Standards, 242; Water Purification, 242; Purification of Sewage, 244; Swimming Pool Sanitation, 244; True-False Test, 244; Completion Test, 245.	

CHAPTER XXI

MILK AND FOOD - - - - -	246
Milk, 246; Bacteria in Milk, 246; Diseases Transmitted by Milk, 247; Characteristics of Milk-Borne Epidemics, 247;	

Pasteurized Milk, 248; Milk Grading, 249; Certified Milk, 250; Pasteurized Versus Raw Milk, 251; Requirements for a Safe Milk Supply, 251; Food, 252; Diseases Transmitted by Food, 252; Food Poisoning, 252; Food Infection, 252; Staphylococcus Food Intoxication, 253; Food Preservation, 253; True-False Test, 254; Completion Test, 254.

SECTION IV SPECIAL BACTERIOLOGY

CHAPTER XXII

THE COLON-TYPHOID GROUP OF ORGANISMS - - - - -	255
<p>The Bacillus of Typhoid Fever, 255; Morphological, Staining, and Cultural Characteristics, 255; Pathogenicity, 256; How Typhoid Bacilli Enter the Body, 256; Distribution of Bacilli in the Body, 257; How Typhoid Bacilli Leave the Body, 257; How Typhoid Fever Is Spread, 257; Antibody Formation, 258; Immunity, 259; Laboratory Diagnosis, 259; The Prevention of Typhoid Fever, 260; Vaccination to Prevent Typhoid Fever, 262; The Paratyphoid Bacilli (A and B), 263; The Colon Bacilli, 263; The Dysentery Bacilli, 264; Pathogenicity, 265; Mode of Infection, 265; Distribution of Bacilli in the Body, 265; Laboratory Diagnosis, 265; Immunity, 265; Prevention, 265; Vaccine and Serum Therapy, 266; The Summer Diarrheas of Infants, 266; Questions for Review, 266; True-False Test, 266; Completion Test, 267.</p>	

CHAPTER XXIII

THE ACID-FAST BACTERIA - - - - -	269
<p>Mycobacterium Tuberculosis, 269; Importance and Distribution, 269; General Characteristics of Mycobacterium Tuberculosis, 270; Types of Tubercle Bacilli, 271; Toxic Products of Tubercle Bacilli, 272; Sources and Mode of Infection, 273; Spread of Mycobacterium Tuberculosis Within the Body, 275; Effects of Tubercle Bacilli on the Body, 275; Tuberculous Infection Versus Tuberculous Disease, 275; Immunity, 275; Laboratory Diagnosis, 277; Prevention, 279; Specific Therapy, 280; Mycobacterium Leprae, 281; Mode of Infection, 281; Laboratory Diagnosis, 282; Prevention and Control, 282; The Smegma Bacillus (Mycobacterium Smegmatis), 282; Questions for Review, 283; True-False Test, 283; Completion Test, 283.</p>	

CHAPTER XXIV

	PAGE
BACTERIA PRODUCING EXTRACELLULAR TOXINS - - - - -	285
The Bacillus of Diphtheria (<i>Corynebacterium Diphtheriae</i>), 285; General Characteristics, 285; Toxin of <i>C. Diphtheriae</i> , 287; Pathogenicity, 287; Sources and Mode of Infection, 288; Diphtheria Carriers, 288; Bacteriological Diagnosis, 289; Diphtheria Antitoxin, 290; Immunity, 291; Toxin-Antitoxin, 291; Diphtheria Toxoid, 292; The Schick Test, 292; Specific Therapy of Diphtheria, 293; Prevention and Control of Diphtheria, 294; Diphtheroid Bacilli, 295; The Bacillus of Tetanus (<i>Clostridium Tetani</i>), 296; General Characteristics, 296; Distribution, 296; Toxin Production, 297; Pathogenicity, 297; Source and Mode of Infection, 298; Immunity, 299; Prevention and Treatment, 299; The Bacilli of Gas Gangrene, 300; The Bacillus of Botulism (<i>Clostridium Botulinum</i>), 301; Questions for Review, 303; True-False Test, 303; Completion Test, 304.	

CHAPTER XXV

THE GRAM-POSITIVE COCCI - - - - -	305
The Diplococcus of Pneumonia (the <i>Pneumococcus</i>), 305; General Characteristics of the <i>Pneumococcus</i> , 305; Types of <i>Pneumococci</i> , 306; Toxin Production, 307; Pathogenicity, 307; Mode of Infection, Epidemiology, 307; Immunity, 308; Laboratory Diagnosis, Determination of Types, 308; Differentiation of <i>Pneumococci</i> and <i>Streptococci</i> , 309; Specific Therapy, 311; Prevention, 311; Other Causes of Lobar Pneumonia, 311; Other Diseases Caused by <i>Pneumococci</i> , 311; The <i>Streptococci</i> , 312; General Consideration of <i>Streptococci</i> and the Diseases They Cause, 312; General Characteristics, 312; Classification, 313; Poisons Produced by <i>Streptococci</i> , 314; Pathogenicity, 315; Human Diseases Due to <i>Streptococci</i> , 315; <i>Streptococcus</i> Infections in Lower Animals, 316; Source and Mode of Infection, 316; Laboratory Diagnosis, 317; Immunity, 317; Prevention, 317; Specific Therapy, 317; The <i>Streptococcus</i> of Scarlet Fever, 318; Source and Mode of Infection, 318; The Toxin of Scarlet Fever <i>Streptococci</i> , 318; Immunity, 319; The Dick Test, 319; The Schultz-Charlton Phenomenon, 320; Antitoxin, 320; Specific Therapy, 320; Prevention, 320; Erysipelas, 321; Mode of Infection, 321; Immunity, 322; Rheumatic Fever, 322; Puerperal Sepsis, 322; Septic Sore Throat, 322; <i>Staphylococci</i> , 323; General Characteristics, 323; Classification, 323; Pathogenicity, 324; Toxic Products of <i>Staphylococci</i> , 324; Sources and Mode of Infection, 324; Diseases Caused by <i>Staphylococci</i> , 324; Bacteriological Diagnosis, 325; Immu-	

nity, 325; Specific Therapy, 325; Micrococcus Tetragenus, 325; Questions for Review, 326; True-False Test, 326; Completion Test, 326.

CHAPTER XXVI

THE GRAM-NEGATIVE COCCI - - - - -	328
The Gonococcus, 328; General Characteristics, 328; Pathogenicity, 330; Sources and Mode of Infection, 330; Spread of Gonorrhea in the Body, 331; Laboratory Diagnosis, 331; Economic and Social Importance of Gonorrhea, 332; Immunity, 333; Prevention, 333; The Meningococcus, 334; General Characteristics of the Meningococcus, 334; Meningococci and Gonococci Compared, 335; Types of Meningococci, 335; Toxin Production, 335; Pathogenicity, 336; Source and Mode of Infection, 336; Immunity, 337; Laboratory Diagnosis, 337; Specific Therapy, 338; Prevention, 338; Micrococcus Catarrhalis, 339; Questions for Review, 339; True-False Test, 340; Completion Test, 340.	

CHAPTER XXVII

THE HEMOGLOBINOPHILIC BACILLI - - - - -	341
The Influenza Bacillus (<i>Hemophilus Influenzae</i>), 341; Characteristics of <i>H. Influenzae</i> , 341; The Pertussis Bacillus (<i>Hemophilus Pertussis</i>), 342; Characteristics of <i>H. Pertussis</i> , 343; Pathogenicity, 343; Mode of Infection, 343; Diagnosis, 344; Immunity, 344; Specific Therapy, 344; Prevention, 344; The Bacillus of Duersey, 345; Other Hemoglobinophilic Bacteria, 346; Koch-Weeks Bacillus, 346; Morax-Axenfeld Bacillus, 346; Questions for Review, 346; True-False Test, 346; Completion Test, 346.	

CHAPTER XXVIII

MISCELLANEOUS BACTERIA AND BACTERIAL INFECTIONS - - - -	348
Anthrax, 348; The Anthrax Bacillus, 348; Mode of Infection, 348; Specific Therapy, 349; Prevention, 349; Asiatic Cholera, 350; Cause, 351; Immunity, 351; Plague, 351; Past. Pestis, 352; Clinical Types of Plague, 352; Mode of Infection, 352; Immunity, 353; Laboratory Diagnosis, 353; Specific Therapy, 353; Prevention, 354; Tularemia, 354; Pasteurella Tularensis, 354; Clinical Types of Tularemia, 355; Mode of Infection, 355; Laboratory Diagnosis, 356; Immunity, 356; Specific Therapy, 356; Prevention, 356; Brucellosis (Undulant Fever), 357; General Characteristics of Brucella, 357; Pathogenicity, 358; Source and Mode of Infection, 358; Laboratory Diagnosis, 358; Immunity, 359; Specific Therapy, 359; Prevention, 359; Glanders (Farcy),	

359; *Pseudomonas Pyocyanea*, 360; Bacilli of the *Proteus* Group, 360; The Friedländer Bacilli, 361; Questions for Review, 361; True-False Test, 362; Completion Test, 362.

CHAPTER XXIX

DISEASES CAUSED BY FILTRABLE VIRUSES - - - - -	364
Smallpox (<i>Variola</i>), 365; Measles (<i>Rubeola</i>), 369; German Measles, 371; Epidemic Parotitis (Mumps), 372; Influenza, 372; Swine Influenza, 374; The Common Cold, 374; Poliomyelitis (Infantile Paralysis), 375; Epidemic Encephalitis, 377; Rabies (<i>Hydrophobia</i>), 378; Yellow Fever, 380; Dengue Fever, 381; Infectious Hepatitis—Homologous Serum Jaundice, 382; Venereal Lymphogranuloma, 382; Virus Pneumonia, 383; Other Diseases Caused by Filtrable Viruses, 383; Questions for Review, 383; True-False Test, 384; Completion Test, 384.	

CHAPTER XXX

BACTERIOPHAGE - - - - -	386
-------------------------	-----

CHAPTER XXXI

DISEASES CAUSED BY RICKETTSIAE - - - - -	388
Typhus Fever, 388; Rocky Mountain Spotted Fever, 389; Trench Fever, 390; Other Diseases Caused by <i>Rickettsiae</i> , 390; True-False Test, 390; Completion Test, 391.	

CHAPTER XXXII

SPIROCHETES AND ALLIED ORGANISMS - - - - -	392
Syphilis, 392; <i>Treponema Pallidum</i> , 392; Acquired Syphilis, Mode of Infection, 393; Evolution of a Typical Case, 394; Prenatal (Congenital) Syphilis, 395; Immunity, 395; Laboratory Diagnosis, 396; Prevention, 397; Relation Between Syphilis and Yaws, 397; Relapsing Fever, 397; Rat-Bite Fever, 398; Infectious Jaundice, 398; Fusospirillary Infections, 398; Other Spirochetes and Related Organisms, 400; Questions for Review, 400; True-False Test, 400; Completion Test, 400.	

CHAPTER XXXIII

FUNGI - - - - -	402
General Characteristics, 402; Molds, 402; Conditions Affecting Growth of Molds, 403; Reproduction of Molds, 403; Classification of Molds, 404; Importance of the Common Molds, 404; Yeasts, 405; General Characteristics, 405; Reproduction of Yeasts, 405; Classification of Yeasts, 406; Fermentation, 406; Conditions Affecting Growth of Yeasts, 407; Economic Importance of Yeasts, 407; Diseases Caused by Fungi, 407; The Dermatomycoses, 407; Actinomycosis, 409; Sporotrichosis, 411; Blastomycosis, 411; Coccidioidal	

Granuloma, 412; Torula Infections, 412; Monilia Infections, 413; Thrush, 413; Bronchial and Pulmonary Moniliasis, 413; Sprue (Psilosis), 413; Ergotism, 414; Molds and Plant Diseases, 414; Questions for Review, 415; True-False Test, 415; Completion Test, 415.

CHAPTER XXXIV

THE PROTOZOA - - - - -	416
General Characteristics, 416; Structure of Protozoa, 416; Nutrition, 416; Motility, 418; Cyst Formation, 418; Reproduction, 419; Classification, 419; Diseases Caused by Protozoa, 419; Malaria, 419; Types of Malaria, 420; Mode of Infection, 420; Development of the Parasite in Man, 420; Development of the Parasite in the Mosquito, 421; Cause of Symptoms, 421; Laboratory Diagnosis, 423; Immunity, 423; Mosquitoes Transmitting Malaria, 423; Prevention, 425; Trypanosomiasis, 425; African Trypanosomiasis, 426; South American Trypanosomiasis, 426; Kala-Azar, 427; Amebiasis, 427; Endameba Histolytica, 427; Life History of E. Histolytica, 428; Source and Mode of Infection, 429; Lesions Produced by E. Histolytica, 429; Laboratory Diagnosis, 430; Prevention, 430; Intestinal Flagellates and Ciliates, 430; Vaginal Trichomonas, 430; Questions for Review, 430; True-False Test, 431; Completion Test, 431.	

CHAPTER XXXV

RECOMMENDED METHODS OF INOCULATION TO PREVENT DISEASE -	433
Recommended Methods of the American Public Health Association, 433; Recommended Methods of the Committee on Therapeutic Procedures for Acute Infectious Diseases of the American Academy of Pediatrics, 434; United States Military Personnel, 436.	

PART II PATHOLOGY

CHAPTER XXXVI

PATHOLOGY: DIVISIONS AND IMPORTANCE - - - - -	439
---	-----

CHAPTER XXXVII

THE HOSPITAL PATHOLOGIST AND HIS WORK - - - - -	441
The Clinical Pathologist, 441; The Surgical Pathologist, 442; The Autopsy and the Autopsy Pathologist, 448.	

CHAPTER XXXVIII		PAGE
THE NATURE AND CAUSES OF DISEASE - - - - -		450
The Nature of Disease, 450; The Cellular Concept of Disease, 450; What Disease Is, 450; Structural and Functional Changes, 451; The Interdependence of Organs, 451; The Manifestations of Disease, 451; Etiology and Pathogenesis of Disease, 452; Classification of Diseases, 452; The Causes of Disease, 452; Predisposing Causes of Disease, 452; Immediate or Exciting Causes of Disease, 456; Questions for Review, 459; True-False Test, 459.		
CHAPTER XXXIX		
DEFENSES OF THE BODY AGAINST DISEASE - - - - -		461
General Consideration, 461; Immunity, 463; Phagocytosis, 463; Fever, 463; Questions for Review, 465; True-False Test, 465.		
CHAPTER XL		
DEGENERATIONS, INFILTRATIONS, PIGMENTATIONS, AND CONCRETIONS		466
Degenerations, 466; Cloudy Swelling, 466; Fatty Degeneration, 467; Other Degenerations, 467; Infiltrations, 467; Fatty Metamorphosis (Fatty Infiltration--Fatty Degeneration), 467; Amyloid Infiltration, 468; Calcium Infiltration (Calcification), 468; Uratic Infiltration, 469; Other Infiltration, 469; Pigmentations, 469; Concretions, 470; Questions for Review, 472.		
CHAPTER XLI		
NECROSIS, GANGRENE, AND SOMATIC DEATH - - - - -		473
Necrosis, 473; Gangrene, 474; Somatic Death, 476; Vital Organs, 476; Signs of Death, 476; Cadaveric Changes, 477; Time of Death, 478; Too Favorable Prognoses to Be Avoided, 478; Questions for Review, 478; True-False Test, 479; Completion Test, 479.		
CHAPTER XLII		
DISTURBANCES OF CIRCULATION - - - - -		480
Hyperemia, 480; Active Hyperemia, 480; Passive Hyperemia, 480; Local Anemia (Ischemia), 482; Hemorrhage, 482; Edema, 483; Thrombosis, 484; Embolism, 487; Questions for Review, 488; True-False Test, 488.		
CHAPTER XLIII		
INFLAMMATION, REPAIR, AND REGENERATION - - - - -		490
Causes of Inflammation, 490; The Inflammatory Exudate, 490; Kinds of Inflammation, 491; Local Changes in Inflammation, 491; Signs of Inflammation, 492; Termination of the Inflammatory Process, 493; Inflammatory Lesions,		

497; Leucocytosis and Fever in Inflammation, 498; Complications of Healing, 499; Chronic Inflammation, 499; Granulomatous Inflammation, 500; Reaction of the Tissues to a Foreign Body, 500; Regeneration, 500; Questions for Review, 501; True-False Test, 501; Completion Test, 502.

CHAPTER XLIV

INFECTIOUS DISEASES - - - - - 503

General Features, 503; Diseases Caused by Streptococci, 504; Scarlet Fever, 504; Acute Rheumatic Fever, 505; The Pneumonias, 505; Lobar Pneumonia, 505; Bronchopneumonia, 508; Epidemic Meningitis, 509; Diseases Caused by the Colon-Typhoid Group of Bacteria, 510; Typhoid Fever, 510; Bacillary Dysentery, 512; Diseases Caused by Acid-Fast Bacilli, 512; Tuberculosis, 512; Spread of Myco. Tuberculosis Within the Body, 513; Pulmonary Tuberculosis, 515; Tuberculous Pleurisy, 518; Tuberculosis of the Intestines, 518; Leprosy, 518; Diseases Caused by Bacteria Producing Extracellular Toxins, 519; Diphtheria, 519; Tetanus, 520; Diseases Caused by Spirochetes, 520; Syphilis, 520; Primary Stage, 520; Secondary Stage, 521; Tertiary Stage, 521; Prenatal Syphilis, 522; Neurosyphilis, 523; Cardiovascular Syphilis, 524; Syphilis of the Lungs, 524; Diseases Caused by Protozoa, 524; Malaria, 524; Questions for Review, 524; True-False Test, 525; Completion Test, 525.

CHAPTER XLV

THE VITAMIN DEFICIENCIES - - - - - 527

General Characteristics of Vitamins, 527; Vitamin A (Anti-xerophthalmic, Anti-infection), 528; Vitamin B Complex, 528; Vitamin C (Antiscorbutic), 528; Vitamin D, 528; Vitamin K, 529; Rickets (Rachitis), 529; Pellagra, 531; Beriberi, 533; Scurvy, 533; True-False Test, 534; Completion Test, 535.

CHAPTER XLVI

DISTURBANCES IN SIZE, GROWTH, AND DEVELOPMENT OF CELLS AND TISSUES - - - - - 536

Atrophy, 536; Hypertrophy, 538; Hyperplasia, 538; Metaplasia, 539; Questions for Review, 539; True-False Test, 539; Completion Test, 540

CHAPTER XLVII

TUMORS - - - - - 541

General Characteristics of Tumors, 541; The Cause of Tumors, 541; Resemblance Between Tumor Cells and Normal Cells, 543; Environmental Control and Functions of Tumors, 543; Nourishment of Tumors, 543; Mode of Growth

of Tumors, 544; Resistance of Tumor Cells, 544; Classification of Tumors, 544; Benign Tumors, 546; Benign Epithelial Tumors, 547; Benign Connective Tissue Tumors, 550; Benign Tumors Composed of Muscle Tissue, 553; The Transformation of Benign Into Malignant Tumors, 553; Malignant Tumors, 554; Malignant Epithelial Tumors, 556; Malignant Connective Tissue Tumors, 559; Other Malignant Tumors, 561; Estimating the Malignancy of a Tumor, 562; Economic Importance and Value of Early Diagnosis in Malignant Tumors, 563; General Facts, 564; Cancer of the Skin, 564; Cancer of the Lip and Mouth, 564; Cancer of the Breast, 565; Cancer of the Uterus, 565; Cancer of the Stomach, 565; Cancer of the Intestines, 565; Cancer of the Rectum, 566; Tumors of the Urinary Tract, 566; Tumors in Children, 566; The Principles of the Radiation Therapy of Malignant Tumors, 566; Cause of Death in Malignant Tumors, 566; Teratomas, 567; Cysts, 567; Questions for Review, 568; True-False Test, 568; Completion Test, 569.

CHAPTER XLVIII

DEFECTS OF BODY DEVELOPMENT - - - - - 571

Abnormalities of Body Size, 571; The Skin and Hair, 571; Freckles and Liver Spots, 571; Albinism, 572; Birthmarks, 572; Ichthyosis, 573; Increased Elasticity of the Skin, 573; Congenital Hypertrichosis and Hypotrichosis, 573; The Face, Eyes, and Mouth, 574; Shape of the Face, 574; Eyes of Different Color, 574; Cross-Eye, 574; Nearsightedness (Myopia) and Farsightedness (Hyperopia), 574; Cataract, 574; Harelip, 575; Tongue-tie, 575; Fistulas and Cysts of the Neck, 575; The Breast (Mammary Gland), 576; The Extremities, 577; Polydactylism, 577; Absence of Hands and Feet, 577; Absence of Arms and Legs, 577; The Internal Organs, 577; Situs Inversus, 577; Intestinal Diverticula, 577; Exstrophy of the Bladder, 577; Heart, 577; Kidneys, 577; Bicornate Uterus, 578; Central Nervous System, 578; Pilonidal Sinus and Cyst, 579; Mongolism, 579; Hydrocephalus, 579; Deaf-Mutism and Color Blindness, 579; Deaf-Mutism, 579; Color Blindness, 580; Aberrant Tissues, 580; Hermaphrodism, 580; Double Monsters, 580; Questions for Review, 581; True-False Test, 582; Completion Test, 582.

CHAPTER XLIX

DISEASES OF THE HEART AND BLOOD VESSELS - - - - - 584

The Heart, 584; Congenital Defects, 584; Hypertrophy and Dilatation of the Heart, 584; Hypertrophy, 584; Dilatation of the Heart, 585; Endocarditis, 587; Valvular Defects of the Heart, 588; Coronary Disease, 590; The Blood Ves-

PAGE

sels, 590; The Arteries, 590; Arteriosclerosis, 590; Aneurysm, 591; The Veins, 593; Varicose Veins (Varix), 593; Questions for Review, 593; True-False Test, 594; Completion Test, 594.

CHAPTER L

THE BLOOD AND ITS DISEASES - - - - -	595
Red Blood Cells and Hemoglobin, 596; Anemia, 597; Secondary Anemia, 598; The Primary Anemias, 599; Leucocytes, 602; Leucocytosis, 602; Leucemia, 605; Infectious Mononucleosis, 606; Blood Platelets, 606; Questions for Review, 607; True-False Test, 607.	

CHAPTER LI

DISEASES OF THE LYMPH NODES AND SPLEEN - - - - -	609
The Lymph Nodes, 609; Enlargement of the Lymph Nodes, 609; Lymphadenitis, 610; Tuberculosis, 610; Syphilis, 611; Hodgkin's Disease, 611; Tumors, 612; Carcinoma, 612; Lymphosarcoma, 613; The Spleen, 613; Questions for Review, 613; True-False Test, 613.	

CHAPTER LII

DISEASES OF THE RESPIRATORY SYSTEM - - - - -	615
The Nose, 615; Rhinitis, 615; Tumors of the Nose, 615; Adenoids, 615; The Larynx, 616; Inflammations, 616; Acute Laryngitis, 616; Diphtheritic Laryngitis, 616; Chronic Laryngitis, 616; The Bronchi, 616; Bronchitis, 616; Bronchiectasis, 617; The Lungs, 617; Circulatory Disturbances, 617; Hemorrhage, 617; Emphysema, 617; Atelectasis, 618; Pneumonia, 618; Tuberculosis, 618; Abscess of the Lungs, 618; Tumors of the Lung, 618; Sputum, 619; General Characteristics, 619; Amount, 619; Appearance and Consistency, 619; Character, 619; Bloody Sputum, 619; Color, 620; Objects Found in Sputum, 620; The Sputum in Disease, 620; Tuberculosis, 620; The Pleura, 621; Hydrothorax, Hemothorax, Pneumothorax, 621; Pleuritis, 621; Questions for Review, 622; True-False Test, 622.	

CHAPTER LIII

DISEASES OF THE NERVOUS SYSTEM - - - - -	624
The Meninges, 624; Hemorrhage, 624; Purulent Meningitis, 624; Tuberculous Meningitis, 625; Syphilitic Meningitis, 626; The Brain, 626; Injuries, 626; Cerebral Concussion, 626; Compression, 627; Circulatory Disturbances, 628; Hydrocephalus, 628; Cerebral Hemorrhage, 630; Thrombosis and Embolism, 630; Inflammations, 631; Encephalitis, 631; Brain Abscess, 632; General Paresis, 633; Epilepsy, 633;	

Brain Tumors, 634; The Spinal Cord, 635; Poliomyelitis, 635; Tabes Dorsalis, 635; The Cerebrospinal Fluid, 636; Characteristics of Normal Fluid, 636; Pathological Changes in the Cerebrospinal Fluid, 636; Color and Appearance, 636; Cells, 637; Cerebrospinal Fluid Changes in Diseases of the Central Nervous System, 637; Purulent Meningitis, 637; Tuberculous Meningitis, 637; Poliomyelitis, 638; Encephalitis, 638; Neurosyphilis, 638; Brain Abscess, 638; Tumors of the Brain and Cord, 638; Questions for Review, 639; True-False Test, 639; Completion Test, 640.

CHAPTER LIV

DISEASES OF THE DIGESTIVE SYSTEM - - - - - 641

The Lip, Mouth, and Tongue, 641; Stomatitis, Glossitis, and Gingivitis, 641; Catarrhal Stomatitis, 641; Aphthous (Phlyctenular or Vesicular) Stomatitis, 641; Ulcerative Stomatitis, 641; Trench Mouth, 642; Thrush (Parasitic Stomatitis), 642; Syphilis of the Lip and Oral Cavity, 642; Tumors of the Mouth, 643; Cancer of the Lip, 643; Cancer of the Tongue, 643; Epulis or Giant Cell Tumor, 644; The Throat, 644; Pharyngitis, 644; Retropharyngeal Abscess, 644; Tonsillitis, 644; Catarrhal Tonsillitis, 644; Lacunar Tonsillitis, 645; Chronic Tonsillitis, 645; Diphtheria, 645; Vincent's Angina, 645; Septic Sore Throat, 645; The Esophagus, 646; Stenosis—Strictures, 646; Tumors, 646; The Stomach and Duodenum, 646; Congenital Defects, 646; Congenital Hypertrophic Stenosis, 646; Gastric Hemorrhage, 647; Peptic Ulcer, 647; Peptic Ulcer of the Stomach (Gastric Ulcer), 648; Duodenal Ulcer, 649; Cancer, 650; Gastric Contents, 651; The Intestines, 654; Congenital and Acquired Abnormalities of Shape and Position, 654; Diverticula, 654; Hernia, 655; Wounds and Ruptures of the Intestines, 657; Communicable Diseases Affecting the Intestines, 657; Intestinal Obstruction, 657; Acute Intestinal Obstruction, 658; Chronic Intestinal Obstruction, 659; Intussusception, 659; Volvulus, 659; Cancer of the Intestine, 660; Intestinal Protozoa, 660; Feces, 660; Color, 660; Mucous, 661; Blood, 661; Concretions, 661; Intestinal Worms, 662; Tapeworms, 662; Hookworm, 665; Strongyloides Intestinalis, 666; Ascaris Lumbricoides (Earthworm, Roundworm), 666; Oxyuris Vermicularis (Threadworm, Pinworm, Seatworm), 666; Trichocephalus Dispar, 667; Flukes, 667; Intestinal Bacteria, 667; The Vermiform Appendix, 667; Appendicitis, 667; Acute Catarrhal Appendicitis, 669; Acute Diffuse Appendicitis, 669; Appendicular Obstruction, 671; Chronic Appendicitis, 671; The Rectum and Anus, 672; Proctitis, 672; Abscesses, 672; Fissure, 673; Fistula, 673; Hemor-

rhoids, 674; Benign Strictures of the Rectum, 675; Pro-lapse of the Rectum, 675; Carcinoma of the Rectum, 675; The Liver, 676; Degenerative Lesions, 676; Fatty Infiltra-tion and Degeneration, 676; Acute Yellow Atrophy of the Liver, 676; Circulatory Disturbances, 677; Portal Obstruc-tion, 677; Infectious Hepatitis, 677; Liver Abscess, 677; Cirrhosis of the Liver, 678; Portal Cirrhosis (Alcoholic Cirrhosis, Hobnail Liver), 678; Biliary Cirrhosis (Hyper-trophic Cirrhosis, Hanot's Cirrhosis), 678; Tumors, 679; The Gallbladder and Bile Ducts, 679; Jaundice (Icterus), 679; Inflammations, 681; Acute Cholecystitis, 681; Chronic Cholecystitis, 683; Gallstones, 683; The Pancreas, 685; Fat Necrosis, 685; Pancreatitis, 686; Relation of the Pancreas to Diabetes Mellitus, 686; The Peritoneum, 686; Ascites, 686; Peritonitis, 686; Acute Peritonitis, 686; Tuberculous Perito-nitis, 688; Abdominal Adhesions, 688; Tumors of the Perito-neum and Neighboring Structures, 688; Questions for Re-view, 689; True-False Test, 689; Completion Test, 690.

CHAPTER LV

DISEASES OF THE URINARY SYSTEM - - - - - 691

The Kidneys, 691; Renal Hemorrhage, 691; Nephritis, 691; Uremia, 693; Tuberculosis of the Kidney, 693; Tumors of the Kidney, 694; Hypernephroma, 694; Congenital Mixed Tumors, 694; The Kidney Pelvis and Ureters, 695; Pyelitis, 695; Hydronephrosis, 696; Pyonephrosis, 696; Renal Calculi, 696; The Bladder, 698; Cystitis, 698; Vesical Calculi, 699; Tumors, 699; The Urethra, 700; Urethritis, 700; Nonspecific Urethritis, 700; Gonorrheal Urethritis, 700; Stricture, 701; Urethral Caruncle, 701; Urine, 701; General Characteristics, 701; Amount, 702; Color, 702; Appearance, 702; Specific Gravity, 703; Reaction, 703; Normal Composition, 703; Abnormal Constituents of Urine, 703; Albumin, 704; Sugar, 704; Indican, 704; Acetone, Diacetic Acid, and Beta-oxybutyric Acid, 705; Hemoglobin, 705; Bile, 705; Casts, 705; Pus, 706; Red Blood Cells, 706; Bacteria, 706; The Urine in Diabetes and Nephritis, 706; Diabetes, 706; Nephritis, 708; Questions for Review, 708; True-False Test, 708.

CHAPTER LVI

DISEASES OF THE FEMALE ORGANS OF REPRODUCTION - - - - - 710

The Ovaries, 710; Inflammation, 710; Ovarian Abscess, 710; Cysts of the Ovary, 710; Follicular Cysts, 710; Corpus Luteum Cysts, 710; Cystadenomas, 710; Multilocular (Pseu-domucinous) Cystadenomas, 712; Papillary (Serous) Cyst-adenomas, 712; Carcinoma, 713; Dermoid Cysts, 713; The

Fallopian Tubes, 714; Salpingitis, 714; Acute Salpingitis, 714; Chronic Salpingitis, 715; Tuberculous Salpingitis, 716; Ectopic Pregnancy, 716; The Uterus, 717; Hemorrhage, 717; Endometritis and Endocervicitis, 718; Acute Endometritis and Endocervicitis, 718; Chronic Endometritis and Endocervicitis, 718; Fibromyomas, 719; Polyps, 721; Carcinoma, 722; Carcinoma of the Cervix, 722; Carcinoma of the Body of the Uterus, 723; Chorionepithelioma, 724; The Vagina, 724; Vaginitis, 724; Acute Catarrhal Vaginitis, 724; Pseudomembranous Vaginitis, 724; Chronic Vaginitis, 724; Trichomonas Vaginitis, 725; Monilia Vaginitis, 725; The Mammary Glands, 725; Acute Mastitis, 725; Chronic Mastitis, 725; Discharges From the Nipple, 726; Fibroadenoma, 726; Carcinoma, 727; Paget's Disease of the Nipple, 729; Cysts, 729; Questions for Review, 729; True-False Test, 730.

CHAPTER LVII

DISEASES OF THE MALE ORGANS OF REPRODUCTION - - - - - 731

The Testis and Epididymis, 731; Inflammations, 731; Acute Epididymitis, 731; Acute Orchitis, 731; Chronic Orchitis, 731; Tuberculosis, 731; Syphilis, 732; Tumors, 732; Hydrocele, 732; Varicocele, 733; The Prostate Gland, 733; Inflammation, 733; Acute Prostatitis, 733; Chronic Prostatitis, 734; Tuberculosis, 734; Enlargement of the Prostate, 734; Cancer, 735; Questions for Review, 735.

CHAPTER LVIII

THE ENDOCRINE GLANDS - - - - - 736

Introduction, 736; The Thyroid Gland, 736; Physiology, 736; Goiter, 737; Hypothyroidism, 738; Hyperthyroidism, 741; Carcinoma, 741; The Parathyroid Glands, 742; The Pituitary Body (Hypophysis), 742; Introduction, 742; Hyperpituitarism, 744; Gigantism, 744; Acromegaly, 744; Hypopituitarism, 745; Dwarfism, 745; Pituitary Cachexia, 745; Diabetes Insipidus, 745; The Adrenal Glands, 745; Addison's Disease, 746; The Thymus, 746; Status Lymphaticus, 746; The Pancreas, 747; Questions for Review, 747; True-False Test, 748; Completion Test, 748.

CHAPTER LIX

DISEASES OF THE BONES AND JOINTS - - - - - 749

The Bones, 749; Inflammations, 749; Tuberculosis, 750; Tuberculosis of the Spine (Pott's Disease), 750; Syphilis, 752; Tumors, 752; Introduction, 752; Benign Tumors, 753; Primary Malignant Tumors, 754; Metastatic Tumors of Bone, 754; The Joints, 755; Acute Arthritis, 755; Chronic Arthri-

tis, 756; Chronic Infectious Arthritis, 756; Osteo-arthritis, 757; Gonorrheal Arthritis, 757; Tuberculous Arthritis, 758; Syphilis of the Joints, 760; Questions for Review, 761.

PART III

LABORATORY EXERCISES

EXERCISES IN MICROBIOLOGY - - - - - 762

General Laboratory Rules, 762; The Microscope, 763; The Cell, 763; General Characteristics of Bacteria, 767; Conditions Affecting Growth of Bacteria, 768; Special Activities of Bacteria, 768; Methods of Studying Bacteria, 770; The Study of Bacteria by Cultures and Animal Inoculation, 771; Destruction of Bacteria by Mechanical and Physical Means, 774; Destruction of Bacteria by Chemicals, 775; Immunity, 776; Hypersensitiveness, 778; How Infection Is Spread, 779; Bacteriology of Water, 780; Bacteriology of Milk, 781; The Colon-Typhoid Group of Bacteria, 781; The Acid-Fast Bacteria, 782; Bacteria Producing Extracellular Toxins, 782; The Pyogenic Cocci, 783; Spirochetes, 784; Fungi, 784; Protozoa, 784.

EXERCISES IN PATHOLOGY - - - - - 785

Degenerations, Infiltrations, Pigmentations, and Concretions, 785; Necrosis, Gangrene, and Somatic Death, 785; Disturbances of Circulation, 785; Inflammation and Repair, 785; Infectious Diseases, 786; Disturbances in the Size, Growth, and Development of Cells, 786; Tumors, 786; Diseases of the Heart and Blood Vessels, 786; Diseases of the Blood, 787; Diseases of the Lymphatic System, 787; Diseases of the Respiratory System, 787; Diseases of the Nervous System, 787; Diseases of the Digestive System, 787; Diseases of the Urinary System, 788; Diseases of the Female Organs of Reproduction, 788; Diseases of the Bones and Joints, 788.

PART IV

GLOSSARY

GLOSSARY - - - - - 789

COLOR PLATES

PLATE	PAGE
I. The Wassermann test - - - - -	206
II. Skin tests for hypersensitiveness - - - - -	228
III. Tubercle bacilli in sputum - - - - -	270
IV. Streptococcus viridans colonies on blood agar - - - - -	314
V. Koplik's spots - - - - -	370
VI. Negri bodies - - - - -	380
VII. Vincent's angina - - - - -	398
VIII. Malarial parasites - - - - -	424
IX. Gangrene of the arm - - - - -	474
X. Section through an ulcer of the stomach - - - - -	498
XI. Tonsillar diphtheria - - - - -	520
XII. Chancre of the upper lip and mucous patches of the tongue - - - - -	522
XIII. Smear of normal blood - - - - -	596
XIV. Blood smear, secondary anemia - - - - -	598
XV. Blood smear, pernicious anemia - - - - -	600
XVI. Blood cells, Giemsa stain - - - - -	604
XVII. Blood smear, myeloid leucemia - - - - -	606
XVIII. Blood smear, lymphatic leucemia - - - - -	606
XIX. Aphthous stomatitis - - - - -	642
XX. Lacunar tonsillitis - - - - -	644
XXI. Ova of intestinal parasites - - - - -	664
XXII. Prolapsing hemorrhoids complicated by cancer of rectum - - - - -	674
XXIII. Jaundice of head and thorax - - - - -	680
XXIV. Dermoid cyst of ovary with twisting of pedicle - - - - -	714
XXV. Hydrosalpinx - - - - -	714

PART I

MICROBIOLOGY

SECTION I

GENERAL PRINCIPLES OF MICROBIOLOGY

CHAPTER I

HISTORY OF MICROBIOLOGY—ITS VALUE

Microorganisms were probably the first living things to appear on the earth and the study of fossil remains indicates that microbial infections and epidemic diseases existed thousands of years ago. That microbes were not seen until less than three centuries ago is because lenses of sufficient power to render them visible were not perfected until that time. Even after microbes were discovered, almost two hundred years elapsed without any great progress in their study being made, and the development of scientific microbiology can be said to be a product of the last seventy-five years.

The magnifying glass was known to the ancients, but the first person to engage in what might be called medical microscopy was Athanasius Kircher, a Jesuit priest, who was well informed in mathematics, physics, medicine, and music, and who first drew attention to the Egyptian hieroglyphics. In 1658 he published a treatise on microscopy in which he recorded seven experiments on the nature of putrefaction. Kircher's microscope magnified only thirty-two times. The modern microscope which magnifies a thousand times or more has been perfected during the last three-quarters of a century.

Among the earliest microscopists was Leeuwenhoek (Lā'-vĕn-hōök'), who is known as "the father of bacteriology" because it was he who first accurately described the different shapes of bacteria and pictured their arrangement in infected

material (1683). Leeuwenhoek was a wealthy man who devoted the major portion of his time to scientific studies. He fashioned his own microscopes and ground most of their lenses himself. Of these microscopes he made about two hundred and fifty. The better ones magnified about one hundred and sixty times. In addition to his work in microbiology Leeuwenhoek made other contributions to medicine; namely, he gave the first complete account of the red blood cells, demonstrated the capillary connections between arteries and veins, and made other important anatomical observations. As has been previously said, almost two hundred years passed between the time of their discovery by Leeuwenhoek and the beginning of the intensive study of microbes and their activities.

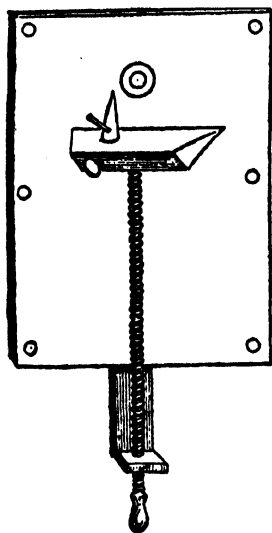


Fig. 1.—Leeuwenhoek's microscope. (From Conn and Conn: *Bacteriology*. Williams and Wilkins Co.)

In 1762 Plenciz, a Viennese physician, published a thesis in which he stated that it was his belief that all infectious diseases were caused by living organisms and that there was an organism for each disease. He also believed that the organisms multiplied within the body and suggested that they might be transferred from person to person by

the air. This is reminiscent of a treatise (*De Contagione*) written by Girolamo Fracastoro in 1546, in which it was declared that diseases were caused by minute seed which might be spread from person to person by direct bodily contact, intervening objects, or through the air.

One of the most epochal contributions to preventive medicine the world has ever known was made on May 14, 1796, when Edward Jenner, having been impressed by the countryside tradition that milkmaids who contracted cowpox while milking were subsequently immune to smallpox, performed a vaccination against smallpox by transferring material from a cowpox pustule on the hand of a milkmaid to the arm of a boy. Six weeks later the boy was inoculated with smallpox and failed to develop the disease. In 1798 he published his results in twenty-three cases. By 1800 about six thousand persons had been inoculated with cowpox to prevent smallpox, and the scientific basis of the method which, in a more refined form, is used today was firmly established.

One of the factors that gave impetus to the rapid development of microbiology that finally came was the argument that had been going on for years concerning spontaneous generation. The proponents of this theory believed that living forms sprang from nonliving matter, and the opponents believed that every living thing descended from parents like itself. The older proponents of the theory believed that eels originated from mud and gave formulas for producing mice from decaying rags and cheese. As time went on, it was conceded that spontaneous generation did not occur in the higher forms of life, but many still held that some forms of microscopic life were products of putrefactive processes. The opponents held that microbes originated in only one way, by the multiplication of their ancestors, and that they were the cause of putrefaction instead of being the result of it. Much experimenting was done on both sides, and the argument went merrily along until Pasteur completely and finally disproved the theory of

spontaneous generation and showed the beliefs of its opponents to be correct.

In the early nineteenth century François Appert laid the foundation upon which modern canning and preserving industries are based by discovering the process of canning.

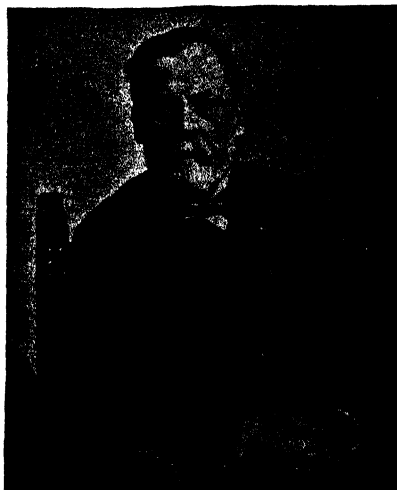


Fig. 2.—Louis Pasteur (1822-1895). (From Garrison: *History of Medicine*. W. B. Saunders Co.)

The development of modern bacteriology began with the work of the great French scientist, Louis Pasteur (1822-1895), who probably has had more influence on future generations than any man that ever lived except Christ. He was born the son of a tanner at Dôle, France, in 1822. He was not a physician but a chemist. At the age of about thirty, having already distinguished himself as a chemist, he became interested in the process of fermentation which, among other things, led to his disproving the theory of spontaneous generation. In 1867 he proved that the "diseases of wine" could be prevented without altering its flavor by heating it, for a short time, to a temperature a little more than halfway between the freezing and boiling point (55° - 60° C.). This process is known as pasteurization and is employed throughout the civilized world today to preserve milk and certain other perishable foods. Pas-

teurization was introduced into the United States on a commercial basis in 1892. Next he proved that pébrine, a disease of silkworms which threatened to destroy the silk industry of France, was due to an animal parasite, and devised methods for its prevention. Later he confirmed Koch's studies on anthrax which was the first animal disease proved to be caused by bacteria. He discovered the staphylococcus, described the pneumococcus, and was codiscoverer of the bacillus of malignant edema. In 1881 he produced anthrax vaccine. The initial demonstration of this vaccine is one of the most dramatic episodes in medical history. His next step and the one for which he is most widely known was the development of the Pasteur treatment for rabies. He gave the first treatment in 1885 and his method, but slightly modified, is used throughout the world today. Pasteur died in 1895 and his body lies in the Pasteur Institute of France.

A bacteriologist second only to Louis Pasteur was Robert Koch (1843-1910), of Germany. His first contribution to the science of bacteriology was the discovery of the anthrax bacillus. This work was quickly confirmed by Pasteur. Koch was the first to stain bacterial smears in accordance with the methods in use today. He devised a liquefiable solid culture medium (gelatin) and worked out methods of obtaining bacteria in pure cultures. The hanging drop method of studying bacteria, as used today, is a product of his genius. In 1882 Koch discovered the tubercle bacillus.

Koch restated certain principles relating to the germ theory of disease with such clarity that they are known today as "Koch's laws" or "Koch's postulates." These postulates held that before a given organism could be said to be the cause of a disease, (1) it must be constantly present in the lesions of the disease, (2) it must be isolated in pure culture, (3) it must produce the disease when inoculated in susceptible animals, and (4) it must be isolated from the lesions of the infected animal. Although it is known that certain human diseases cannot be transmitted to the lower animals and that in some cases other methods of proving the relation between causal agent and disease have been

found, the general principles set forth in Koch's postulates remain to this day the basis of the experimental investigation of infectious diseases.

Joseph Lister (1827-1912), famous English surgeon, was so impressed with the similarity between wound infections and certain fermentative and putrefactive changes which Pasteur had already proved to be caused by microorganisms that he concluded that wound infections, too, were due to microorganisms. With this idea in mind, he protected wounds with dressings saturated with a solution of carbolic acid and devised operating room procedures calculated to destroy the microorganisms. The establishment of these methods was so far-reaching in its effects that Joseph Lister will always be known as "the father of antiseptic surgery."

In 1880 Laveran discovered the parasite of malaria, and within the next year or two its transmission by the mosquito was thoroughly worked out.

From 1882 to 1884, Elie Metchnikoff proposed the phagocytic theory of immunity, and in 1897, Ehrlich proposed the chemical theory. The controversy which raged between the followers of these opposing theories has done much to put immunology on a scientific basis.

The first diphtheria antitoxin was produced on a commercial scale in 1894. The work on which this was based was done in America, but it was perfected in Europe.

In 1896 Gruber and Widal discovered the phenomenon of agglutination. Practical application of this phenomenon resulted in the Widal test for typhoid fever, the typing of sputum in pneumonia, and the agglutination test for such diseases as typhus fever, undulant fever, and tularemia. Not only is this phenomenon of value in the diagnosis of disease, but it is also one of the common procedures in the identification of bacteria. In this same year Wright introduced typhoid vaccination in the English army.

In 1906 Bordet described the phenomenon of complement fixation and, in the same year, Wassermann applied it to the diagnosis of syphilis, giving the medical profession the highly important Wassermann test for syphilis.

The research which led to the discovery of the sulfonamide drugs was begun in 1900, but their real development was brought about by a group of German pathologists in 1932. The first member of this series of drugs became commercially available in 1935.



Dr. Alice C. Evans



Dr. Ruth Tunncliffe

Fig. 3.—Women microbiologists of modern times.

In 1929, Sir Alexander Fleming reported that the mold *Penicillium notatum* elaborated during its growth a substance which was capable of inhibiting the development of certain bacteria. He called this substance *penicillin*. This monumental work went practically unnoticed until 1940 when Florey and Chain made a systematic study of Fleming's findings and produced penicillin in an impure form. In 1939 Dubos and associates discovered *tyrothricin* which was later found to be made up of two constituents—*gramicidin* and *tyrocidine*. Tyrothricin was the first member of the group of agents known as *antibiotics* to be given extensive study and was the first to be produced in a pure state. In 1944, Waksman and Schatz discovered *streptomycin*.

Among Americans who have contributed to the science of microbiology are Sternberg, Welch, Stitt, Smith, and Park. George M. Sternberg, Surgeon General of the U. S. Army, was one of the early American followers of Pasteur. His *Manual of Bacteriology* published in 1893 (the year in which he became Surgeon General) was one of the early landmarks in American bacteriology. Doctor Sternberg was responsible for the establishment of the Army Medical School which was probably the first school of modern hygiene in America.



Fig. 4.—Charles A. Spencer, the first American manufacturer of microscopes. (Courtesy of Spencer Lens Co., Buffalo, N. Y.)

Little more than ten years later E. R. Stitt became instructor in tropical medicine at the Naval Medical School. He was not so much an academic microbiologist as master of laboratory technic and teacher of tropical medicine. His books on laboratory diagnosis and tropical medicine which

appeared many years ago and today are fully revised have profoundly affected the thought of microbiologists not only in America, but throughout the world.

William H. Welch was the dean of the medical department of Johns Hopkins University. He is well known for his original researches in microbiology.

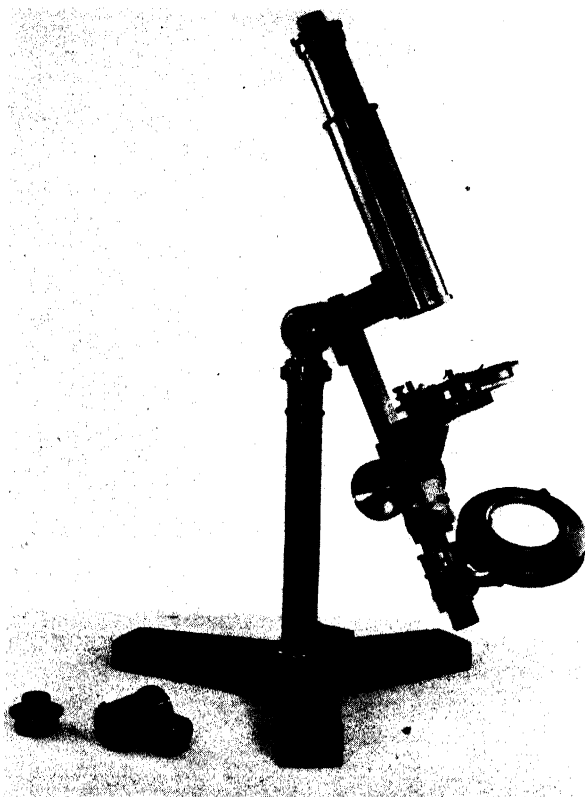


Fig. 5.—Early American microscope. This microscope was manufactured about one hundred years ago. (Courtesy of Spencer Lens Co., Buffalo, N. Y.)

Theobald Smith isolated the organism of bovine tuberculosis and by his studies on Texas fever paved the way for research on insect-borne diseases.

William Hallock Park organized the first municipal bacteriological laboratory in the United States and introduced the routine use of toxin-antitoxin for preventing diphtheria (1914). Just two years before this, the first permanent public health exhibit in the United States was established by the American Museum of Natural History.



Fig. 6.—Students in microbiology laboratory of a modern school of nursing. (Courtesy Parkland Hospital, Dallas, Texas.)

Charles A. Spencer, the first American manufacturer of microscopes, was born at Lennox, New York, 1813. He began the manufacture of microscopes in 1838, and about two years later issued a catalogue listing instruments and supplies. For almost fifty years he developed and manufactured microscopes. His work was carried on by his son, Herbert R. Spencer.

Women have played no inconsiderable part in the development of modern microbiology. Among those who might be mentioned are Ruth Tunnickliff, well known for her studies on streptococci in measles, anaerobic organisms, and phagocytosis; Alice C. Evans, Senior Bacteriologist of the National

Institute of Health and investigator of undulant fever; Georgia Cooper, who classified pneumococci into thirty-two types; and Rebecca Lancefield, who devised the serological classification of streptococci which is widely used at the present time. Gladys Dick with her husband developed our present-day conception of the etiology of scarlet fever as well as immunological methods of diagnosing, preventing, and curing the disease. For many years Anna C. Williams was closely associated with William Hallock Park and was his co-author on the classical textbook, *Pathogenic Microorganisms*. Pearl Kendrick has done extensive research in serology and has added much to our knowledge of whooping cough. Eleanor C. Bliss is well known for her work on streptococci and the sulfonamide drugs.

Among the more recent advances in microbiology which have not been mentioned is the discovery of tularemia in 1910. Another modern advance is the development and practical application of toxoid for the prevention of diphtheria and tetanus. The science of experimental epidemiology in which epidemics are produced and studied in groups of experimental animals had its inception in 1919. Since that time several epidemic diseases have been studied in this manner. Endemic typhus fever was first recognized in America in 1926.

The Value of a Knowledge of Microbiology.—A knowledge of microbiology is of value to every person. It is of special value to physicians, nurses, sanitarians, agriculturists, dairymen, and manufacturers. It is of value to every person because the rules of simple cleanliness rest on the principles of microbiology. Doctors, nurses, and sanitarians must know how disease-producing agents enter the body, how these agents are cast from the body, and how they spread from person to person. Doctors and nurses must know also how infectious agents produce their effects on the body and what steps the body takes to defend itself. In addition, they must know the principles of aseptic technic, how serums and vaccines are made, and how they are used for the prevention and cure of disease.

To the agriculturist a knowledge of microbiology is of importance because upon microbes depend decay and the

fertility of the soil. The dairyman harnesses microbes and uses them in his processes of manufacture. On the other hand, microbes may be enemies that destroy the dairyman's products. The caterer must know how and why his foods spoil, how to prevent this, and what foods may become conveyers of disease. To manufacturers microbes are of importance because they may be used in the manufacture of certain foods and certain articles of raiment. Of all of this we will speak again.

True-False Test

Place the word "true" or "false" before each statement.

- 1. Plenciz, a Viennese physician of the eighteenth century, believed that diseases were caused by living organisms and that there was an organism for each disease.
- 2. Leeuwenhoek gave the first complete account of red blood cells.
- 3. Athanasius Kircher demonstrated the capillary connections between arteries and veins.
- 4. Pasteur was a proponent of the theory of spontaneous generation.
- 5. Louis Pasteur was not a physician but a chemist.
- 6. Koch gave the first treatment for rabies in 1865.
- 7. Koch's "postulates" remain to this day the basis of the experimental investigation of infectious diseases.
- 8. Women have played no significant part in the development of modern microbiology.
- 9. All the sulfonamide drugs became commercially available in 1935.

Completion Test

- 1. Scientific microbiology is a development of the past ----- years.
- 2. The first person to engage in medical microscopy was -----.
His microscope magnified only ----- times.
- 3. The modern microscope magnifies ----- times or more.
- 4. Leeuwenhoek is known as "-----",
-----." He fashioned his own microscopes
and ground most of their lenses.
- 5. In 1796 Edward Jenner made an epochal contribution to preventive medicine when he introduced -----.
- 6. The development of modern bacteriology began with the work of the great French scientist -----
(1822-1895).

7. The process known as _____ which is employed in the preservation of milk and other perishable foods consists of heating to _____° C. for _____ minutes.
8. List the contributions of Robert Koch to microbiology.
 - a. _____
 - b. _____
 - c. _____
 - d. _____
 - e. _____
9. Joseph Lister is known as "_____." Why?
10. The complement fixation test for syphilis is known as the _____ test. It was introduced by _____.
11. Among those who were important in the development of the antibiotics are _____ and _____ whose original research led to their discovery, and _____ and _____ who discovered streptomycin.
12. List some outstanding American contributors to the science of microbiology and tell what they contributed.
13. What are the most recent advances in microbiology?
14. What is the value of a knowledge of microbiology to the nurse? Discuss fully.

References

- Castiglioni, Arturo: A History of Medicine (Translated by E. B. Krumbhaar), New York, 1947, Alfred A. Knopf, Inc.
- Bulloch, William: The History of Bacteriology, New York, 1938, Oxford University Press.
- Gage, S. H.: The Microscope, New York, 1941, Comstock Publishing Co.
- de Kruif, Paul: Microbe Hunters, New York, 1926, Harcourt Brace & Co.
- Zinsser, Hans: Rats, Lice and History, Boston, 1935, Little, Brown & Co.
- Trudeau, Edward Livingston: An Autobiography, Garden City, 1916, Doubleday-Doran & Co.
- Eckstein, Gustav: Noguchi, New York, 1934, Harper & Brothers.
- Epstein and Williams: Miracles From Microbes, New Brunswick, 1946, Rutgers University Press.

CHAPTER II

RELATION OF MICROBES TO OTHER LIVING THINGS—RELATION OF MICROBIOLOGY TO OTHER SCIENCES

All things may be divided into two classes: *animate* (those that have life) and *inanimate* (those that do not have life). Microbes belong to the first class because they are living things. *Biology* is that science which treats of living things in general. That branch of biology which treats of animals is known as *zoology* and that branch which treats of plants is known as *botany*. That branch of biology which treats of unicellular organisms is known as *microbiology*. Not only does it treat of the relation of microbes to disease, but it also treats of their relation to the building up and tearing down processes of Nature, to the fertility of the soil, and to agriculture, industry and art. Microbiology is divided into two parts: *bacteriology* which treats of unicellular plants (bacteria, yeasts, certain molds, etc.) and *protozoology* which treats of unicellular animals (protozoa). The branch of bacteriology that treats of fungi is known as *mycology*.

The branch of microbiology that treats of the relation of microbes to disease is known as *medical microbiology*. Other branches of microbiology are: *sanitary microbiology*, *dairy microbiology*, *food microbiology*, *industrial microbiology*, and *agricultural microbiology*.

When we reach the lower forms of life, it is sometimes difficult to tell whether an organism is an animal or a plant. The popular notion that the essential difference between animals and plants is that animals have the power to move from place to place while plants do not, is not always correct because some plants have the power to move from place to place and some animals are rooted or fixed. In the early days of bacteriology it was thought that bacteria

were animals, but it is now generally agreed that they belong to the plant kingdom.

Principles of Biological Classification.—The basic units used in classifying both plants and animals are:

- | | |
|-----------|------------|
| 1. Phylum | 4. Family |
| 2. Class | 5. Genus |
| 3. Order | 6. Species |

Organisms that reproduce only their exact kind constitute a *species*. For instance the prairie rose and meadow rose are different species of wild rose. Closely related species are grouped in *genera* (plural of genus). Several genera having one or more points of relationship make up a *family*. A group of related families constitute an *order*. Several related orders form a *class*. A number of classes having one or more common characteristics constitute a *phylum*.

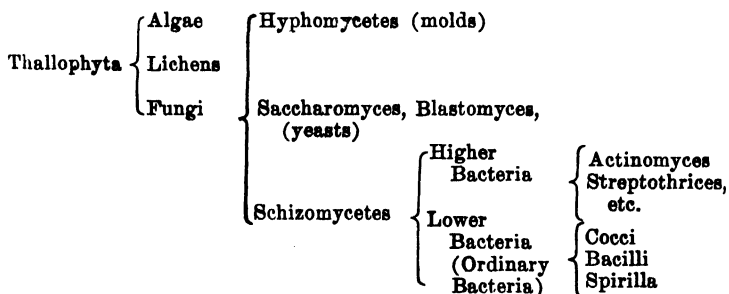
The scientific name of an animal or plant is composed of two words which are Latin in form and frequently represent the name of a person or place with a Latinized termination. The first begins with a capital letter and denotes the genus. The second begins with a small letter and denotes the species. For instance, *Staphylococcus aureus* indicates a bacterium (singular of bacteria) belonging to the genus *Staphylococcus* and species *aureus*, while *Staphylococcus citreus* indicates a bacterium belonging to the same genus but to species *citreus*. Whether a term indicates a class, order, or family may be determined from its ending. Classes end in *etes*; orders end in *ales* and families end in *aceae*. For instance, *Schizomycetes* is the name of a class, *Eubacteriales* is the name of an order, and *Bacteriaceae* is the name of a family.

Animal and plant classification is based almost entirely upon morphology, but the morphology of bacteria as a whole is so uniform that it is useful only in dividing them into comparatively large groups. For more exact identification such criteria as staining reaction, cultural characteristics, biochemical behavior, immunological characteristics, etc., must be used.

Relation of Bacteria to Other Plants.—The plant kingdom is divided into four phyla:

1. Spermatophyta—Seed-bearing plants.
2. Pteridophyta —Ferns and their allies.
3. Bryophyta —Mosses, etc.
4. Thallophyta —Thallus plants.

Thallophytes may be defined as simple forms of plant life which do not differentiate into roots, stems, and leaves. This group is of special importance because it is to it that the unicellular plants belong. The following outline shows the relation existing between the members of this group:



Algae are simple plants many of which are microscopic in size and are shaped like bacteria but differ from bacteria in that they (algae) contain chlorophyl. *Algae* are most often seen in the form of pond scums, seaweeds, etc. *Lichens* are often seen as a scalelike growth on tree trunks and rocks. They contain chlorophyl. *Fungi* are more simple forms of life than the algae and lichens. They do not contain chlorophyl. Although the lower bacteria are fungi they are usually discussed as a separate class, and the term "fungi" as ordinarily used refers to the molds, yeasts, higher bacteria, etc., but not to the lower bacteria.

Lower Forms of Animal Life.—The animal kingdom is divided into from twelve to twenty phyla, depending on the classification used. Regardless of the system of classification used, the simplest forms of animal life are placed in the phylum Protozoa or unicellular animals. The protozoa are of medical interest because some of the most im-

portant disease-producing organisms belong to this group. Example—organisms causing malaria, amebic dysentery, trypanosomiasis, etc.

Questions for Review

1. Into what two classes are all things divided? Define them.
2. What is biology?
3. Into what two branches is biology divided? Of what does each treat?
4. What is microbiology? Into what two branches is it divided? Of what does each treat?
5. Are bacteria animals or plants? Have they always been so considered?
6. How is the scientific name of an animal or plant derived?
7. What are protozoa? Name some diseases caused by protozoa.
8. What indicates whether a term refers to a class, order, or family? Illustrate.

References

- White, E. Grace: General Biology, St. Louis, 1946, The C. V. Mosby Co.
Zinsser and Bayne-Jones: Textbook of Bacteriology, New York, 1939, D. Appleton-Century Co.

CHAPTER III

THE EQUIPMENT OF THE MICROBIOLOGIST

The microbiologist has many instruments of precision at his command. Some of these are in constant use while others are used only in special investigations. A few will be described in the following paragraphs and as many as space permits will be listed at the end of the chapter. Others are described elsewhere in this book.

I. The Microscope

General Description.—The instrument that the microbiologist uses most often and the one that should be handled with the greatest of care is the microscope. Needless to say its workmanship should be of the highest quality. Microscopes are of two kinds, simple and compound. A *simple* microscope is little more than a magnifying lens. A *compound* microscope consists of two or more lens systems in which the magnification of one system is further magnified by the other. A compound microscope consists of two parts, the supporting stand and the optical system. The supporting stand consists of (1) a base and pillar, (2) an inclination joint for tipping the instrument, (3) an arm which supports the optical system and houses the fine adjustment, (4) the stage upon which the object to be examined rests, and (5) a condenser and mirror which are fitted beneath the stage. The condenser and mirror focus the light through a central opening in the stage upon the object to be examined.

The optical system is connected to the arm of the supporting stand by an *intermediate slide* which moves up and down upon the arm in response to the movement of the fine adjustment. The intermediate slide contains the rack and pinion for coarse adjustment which acts directly on the tube of the optical system. The optical system consists of a telescoping tube (drawtube) which supports the *ocular* (eyepiece) at the top and to the bottom of which the *objectives*

are attached by means of a revolving *nose piece*. The stage of the microscope is usually equipped with a *mechanical stage* which firmly holds the slide upon which the object is mounted and allows it to be moved from place to place by set screws. The advantages of a mechanical stage are that the specimen may be examined systematically, and if the examiner is called away from the microscope the specimen remains in its exact position.

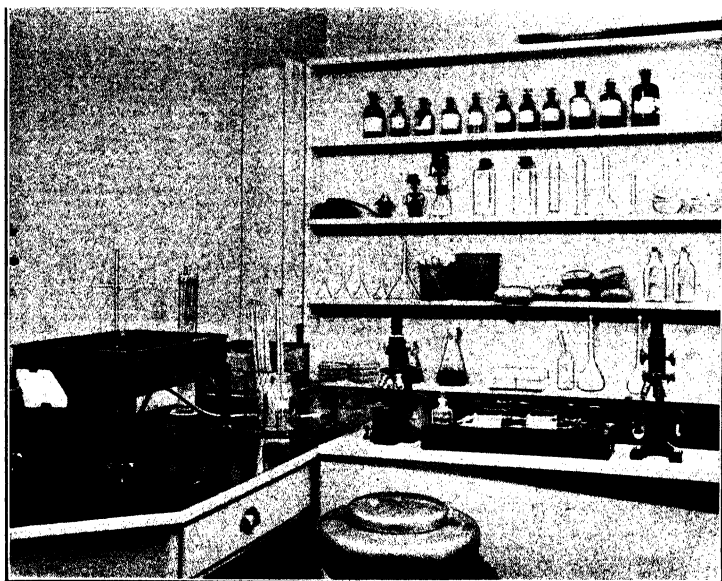


Fig. 7.—A corner in a microbiologist's laboratory. On the work table at the left are two water baths, a Bunsen burner and bacteriological pipettes. On the top shelf are bottles of stain. On the next shelf, from left to right, are a dark-field illuminator, two Seitz filters, two Berkefeld filters, graduated, volumetric flask and evaporating dishes. Funnels, tubes of culture medium, wrapped sterile supplies and dilution bottles are on the second shelf from the bottom. On the bottom shelf are Petri dishes, flasks of culture medium and boxes of slides. At the front are microscopes, staining racks and staining jars, and (lower) the top of a centrifuge.

The magnification of an objective is usually designated by its equivalent focal distance in inches or mm. The higher the number of the objective the less its magnification. American microscopes are usually fitted with 16 mm., 4 mm., and 1.8 mm. objectives. The latter is known as an immersion

objective because for the best results there must be a liquid between the objective and the object being examined. Most immersion objectives use oil of cedarwood. The 16 mm. objective magnifies 10 times, the 4 mm. magnifies 44 times and the 1.8 magnifies 95 times.

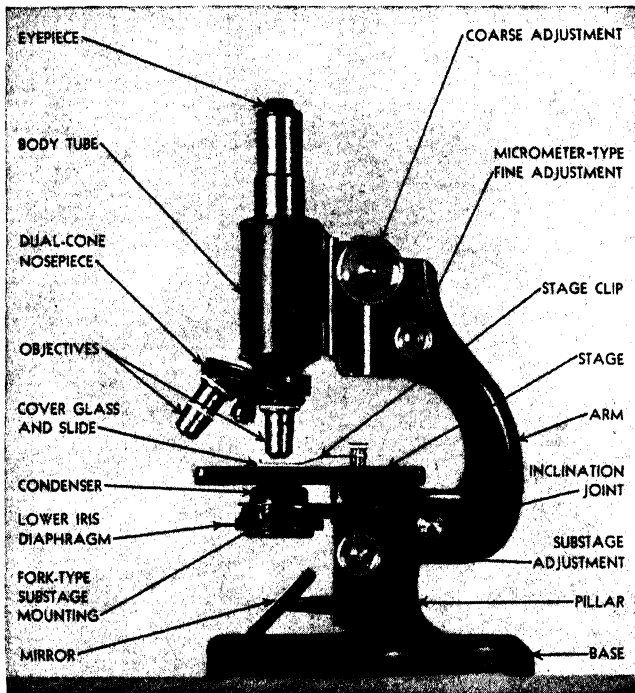


Fig. 8.—Illustration showing the different parts of the microscope. (Courtesy of Spencer Lens Co., Buffalo, N. Y.)

The oculars of a microscope are designated 6 \times , 10 \times , etc., which indicates that they increase the magnification of the objective 6, 10, etc., times, respectively. To obtain the magnification of any combination of ocular and objective multiply the magnification of the objective by that of the ocular. For instance a 10 \times ocular and a 1.8 mm. objective will give a magnification 950 while a 6 \times ocular and a 4 mm. objective will give a magnification of 264. In this connection it should be remembered that magnification means

length. For instance a magnification of 100 means that the object is made to appear 100 times as long and 100 times as wide.

Care and Use of the Microscope.—1. Make it a habit to keep both eyes open. A very little practice will enable one to do this.

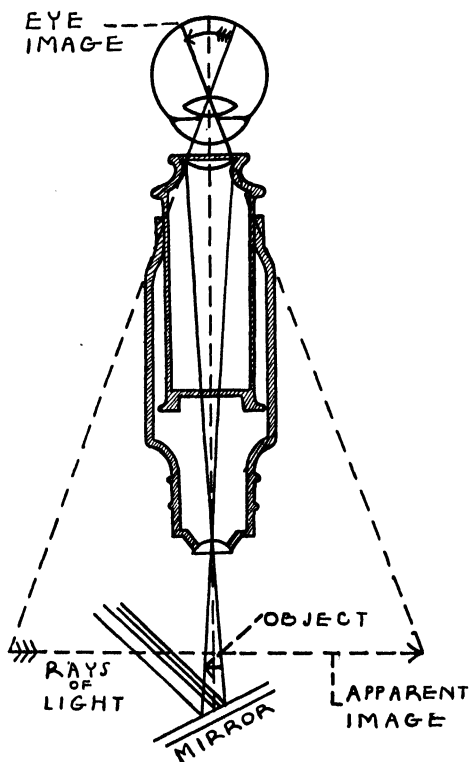


Fig. 9.—Diagram showing how a microscope magnifies. The apparent image is approximately 5 cm. in length. Assume that the object is 50 microns in length and calculate the magnification.

2. Avoid direct sunlight. North light is advantageous. Best results are probably obtained by using a “daylight” microscope lamp.

3. When a slide is placed on the stage see that it lies flat against the stage. Adjust the light so that object is evenly illuminated. Focus down by means of the coarse adjust-

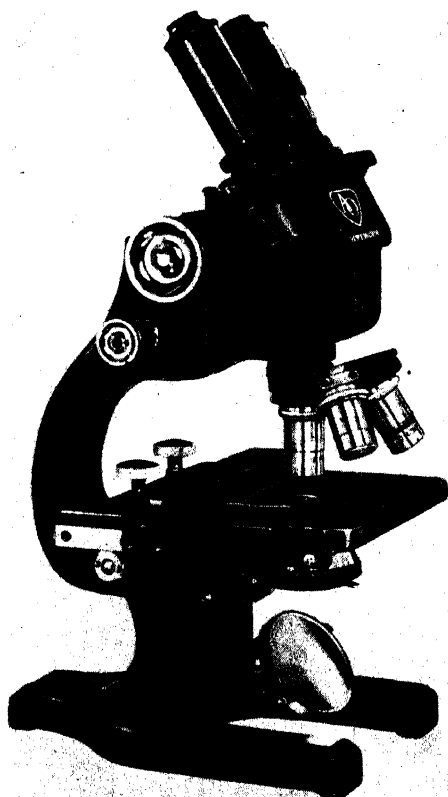


Fig. 10.—Binocular microscope. (Courtesy of Spencer Lens Co., Buffalo, N. Y.)

ment until the objective nearly touches the cover glass but be careful not to touch it. Then focus up until the object comes plainly into view. Complete focusing with fine adjustment. Beginners should learn to focus with the low power objectives. When using the immersion objective place a drop of immersion oil on the object before focusing.



Fig. 11.—Proper position at microscope. The microscope stands straight up on the table and the observer sits squarely in front of it. The left hand on the fine adjustment keeps the object being examined in focus and the right hand manipulates the mechanical stage to bring different portions of the object into view. To avoid eyestrain, both eyes should be kept open when looking in the microscope.

4. Keep the microscope clean and handle all parts with care. Glass parts should not be touched with the fingers. No chemicals should be allowed to come in contact with the microscope because they may injure the finish. The mechanical parts may be cleaned by rubbing with olive oil on gauze and wiping oil off with chamois or lens paper. Remove oily substances from glass parts by wiping with a

lens paper moistened with xylol. This must be done as rapidly as possible to prevent injury to the settings.

5. When through with the microscope clean thoroughly. Put objectives in such a position that the lowest power is in the working position. This is done because if the optical system is accidentally jammed down, the least expensive objective would be injured. Keep microscope covered with bell jar when not in use.

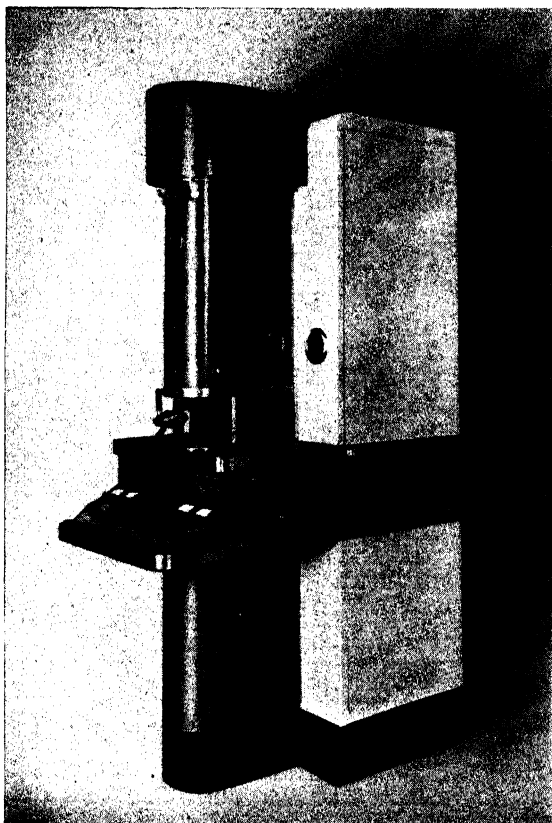


Fig. 12.—Electron microscope. (Courtesy RCA Victor Corporation.)

The Electron Microscope.—The electron microscope, which has become commercially available within the last few years, promises to be of great value in microbiological research. The electron microscope differs from the ordinary microscope

in that, in the latter, rays of ordinary light pass from the object being examined to the eye, while in the electron microscope electrons pass through the specimen and are then focused on a viewing screen. The nature of light is such that it is not possible to get a clear image with an ordinary

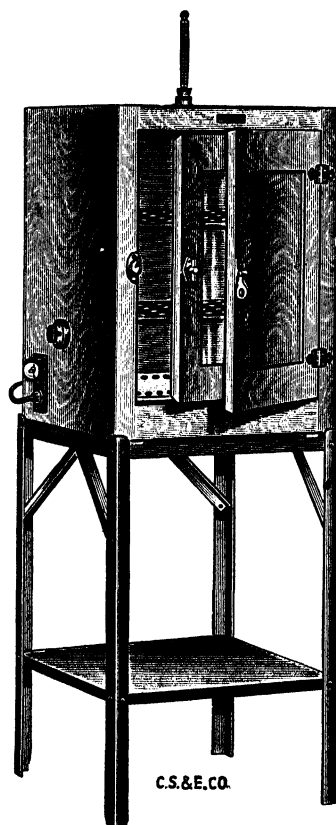


Fig. 13.—Electric incubator. Note double doors (the inner one of glass) and shelves for cultures. (Chicago Surgical and Electrical Co.) (Courtesy of Greene Bros., Dallas, Texas.)

microscope when the magnification is more than 2,000 diameters, but with an electron microscope a magnification of 20,000 diameters is easily obtained. This is of great value in studying the internal structure of microbes; however, like many other instruments of precision, the electron microscope has its limitations.

The Photomicrographic Camera.—Another instrument which is of great value to microbiologists is the photomicrographic camera, with which pictures of objects seen with the microscope are made. This gives an easily preserved visual record of microscopic findings and renders a wealth of microscopic material available for future study.

II. The Bacteriological Incubator

The bacteriological incubator consists of an insulated cabinet fitted with a heating element and a thermostat that cuts the heat off when the temperature reaches the point for which the thermostat is set, and turns it on again when the temperature falls slightly below that point. Good

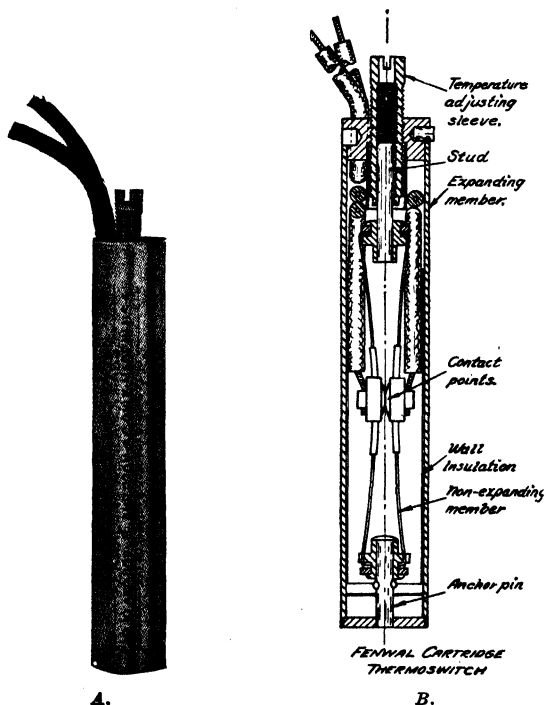


Fig. 14.—A. Fenwall electric thermoregulator. B. Sectional drawing of A. The two pieces of metal that hold the contact points are thermally inert and are mounted in a tube made of heat-sensitive metal. When the tube becomes warmer its length increases. As the length of the tube increases the curvature of the strips of metal which bear the contact points is decreased. This pulls the contact points apart and cuts off the electric current going to the heating element. Note electric wiring to contact points. (The Fenwall Co., Ashland, Mass.) (Courtesy of Greene Bros., Dallas, Texas.)

thermostats placed in a properly constructed incubator will maintain a temperature that varies less than 0.5° C. from day to day. Most incubators are electrically heated. A few use other fuels. The latter do not maintain as constant a temperature as the former. The incubator must be properly ventilated. It is fitted with perforated shelves and many have double doors, the inner one being of glass so that the contents of the incubator may be viewed without admitting cold air. Another incubator is shown in Fig. 26, page 81.

III. Constant Temperature Water Bath

A constant temperature water bath is a metal box which contains a heating element and a thermostat that keeps the water in the box at a constant temperature. Water baths

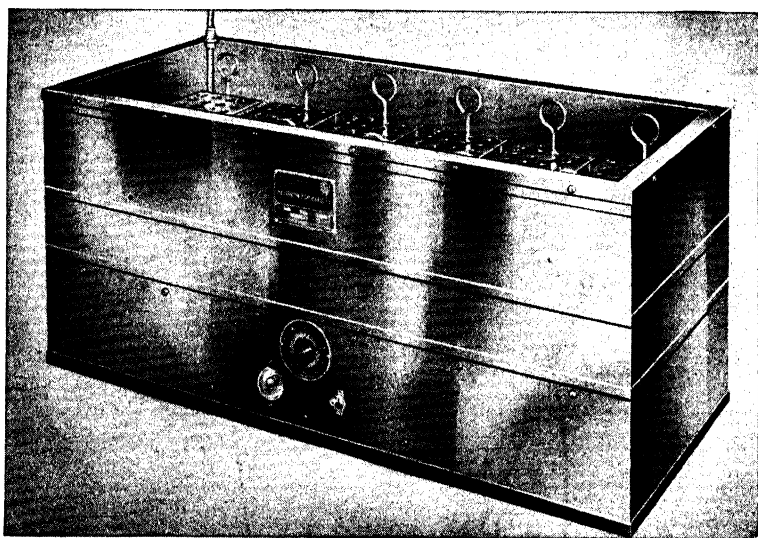


Fig. 15.—Water bath. Note racks for holding test tubes. The bath is filled with water until it rises almost to the top of the racks. The water is held at a constant temperature by means of an electric heating mechanism and thermoregulator. (The Precision Scientific Co., Chicago.) (Courtesy of Greene Bros., Dallas, Texas.)

are usually used for keeping the material in test tubes at a constant temperature as in the Wassermann test, Widal tests, etc.

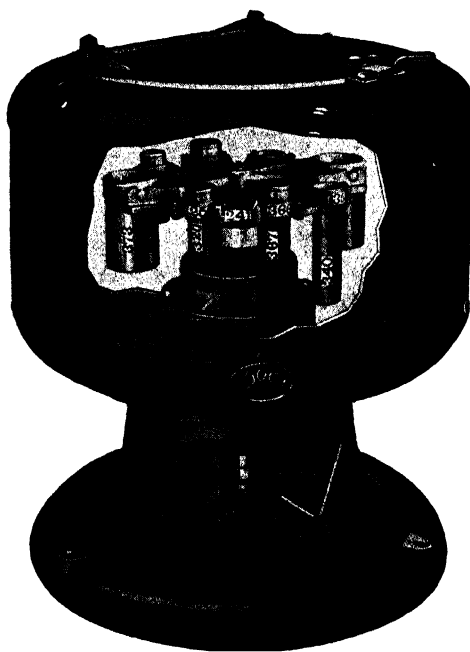


Fig. 16.—Centrifuge. The protective housing has been cut to show the head. The head is fitted with several types of cups which are designed to fit different kinds of containers of the material to be centrifuged. Note lower end of vertical motor and brake in base of centrifuge. (International Equipment Co., Boston, Mass.) (Courtesy of Greene Bros., Dallas, Texas.)

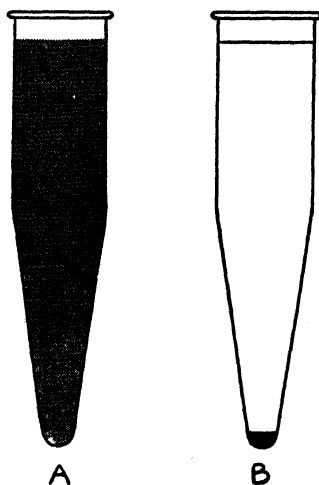


Fig. 17.—Drawing showing the effect of centrifugalization. *A*. Un-centrifuged specimen of a liquid containing particulate matter. Note that the particulate matter is evenly suspended in the liquid. *B*. Same specimen after centrifugalization. Note particulate matter packed in bottom of tube and clear liquid above.

IV. Centrifuge

A centrifuge is a machine that separates particulate matter from a suspension by means of centrifugal force. It consists of, first, a "head" which is rapidly revolved by an upright motor. To the head are attached metal cups for holding tubes or other containers of the material from which the particulate matter is to be separated. When centrifugalization is complete the particulate matter is in the bottom of the container.



Fig. 18.—Washing glassware. Clean glassware is a primary requisite for accurate investigations in microbiology. Disaster is certain to follow if the care of laboratory glassware is placed in inexperienced hands.

V. Sterilizing Equipment

The sterilizing equipment of the microbiological laboratory consists of autoclaves for sterilizing by steam under pressure (Figs. 53 and 54, pages 138 and 139), Arnold sterilizers for sterilizing by free flowing steam (Fig. 52, page 137), dry air sterilizers (Fig. 55, page 142) and apparatus for sterilizing by filtration (Fig. 51, page 136).

VI. Refrigerator

A good refrigerator is necessary in order to preserve specimens, cultures and reagents.

VII. Other Essential Equipment

Platinum loop	Stains
Slides and cover glasses	Balances for weighing
Culture tubes	Graduates
Culture media	Funnel flasks
Petri dishes	Cotton, absorbent and non-absorbent
Dark field illuminator	Thermometers
Fermentation tubes	Bunsen burners
Pipettes	Staining jars and racks
Animal cages	Burettes
Anaerobic jars	Suction pumps
Test tube racks	Bell jars
Hot plates	Culture slides
Hydrogen ion apparatus	Slide boxes
Magnifying glasses	Colony counter
Test tube baskets	

References

- Gage, S. H.: The Microscope, New York, 1941, Comstock Publishing Co.
- Kolmer and Boerner: Approved Laboratory Technic, New York, 1945, D. Appleton-Century Co.
- Gradwohl, R. B. H.: Clinical Laboratory Methods and Diagnosis, St. Louis, 1948, The C. V. Mosby Co.

CHAPTER IV

THE CELL

Every living thing, plant or animal, is made up of one or many cells. In the higher forms of life multiplied millions of cells arrange themselves into groups for the purpose of performing special functions. In the lowest forms of life the whole organism is composed of but a single cell. Such single-celled organisms are known as *unicellular* organisms. Regardless of how simple or how complex an organism may be, its unit of structure and function is the cell.

Protoplasm.—*Protoplasm* (Greek, basic substance) is a colorless, translucent, viscid substance of a colloid nature that forms the physical basis of all life and all cells. Although each type of cell has its own characteristic kind of protoplasm which varies under different conditions, protoplasm is alike in all forms of life so far as the essential characteristics that make it alive are concerned. It is made up principally of water, but many complex substances are a part of it. Within its groundwork are seen numerous granules, clear spaces, and vacuoles. Protoplasm is most likely ordinary matter that has assumed a peculiar structural pattern in which it displays those phenomena characteristic of life. Chemically protoplasm may be defined as a *system of chemical compounds held together in a colloidal suspension and containing among other elements carbon, hydrogen, oxygen and nitrogen in the form of proteins, carbohydrates and fats.*

Size and Shape of Cells.—Excluding the eggs of various animals, cells are of microscopic size, and some are so small that they can scarcely be seen with the highest power of the microscope. A special unit of measurement has been devised for their study. It is the micromillimeter which is $1/1,000$ of a millimeter or $1/25,000$ of an inch in length. It is spoken of as the *micron* and is designated by the Greek letter *Mu* (μ). The paper on which this book is printed is about 100μ in thickness. Although cells show considerable variation in size, it may be said that the average cell is

about seven microns in diameter. Individual variations in the size of organisms of the same species depend on the number, not size, of their cells. Depending on their relation to other cells and their function, cells show marked variation in shape, being spherical, oblong, columnar, or spindle-shaped.

Structure of Cells.—If we examine a typical cell, we will see that its central portion is occupied by a deeply staining structure, known as a *nucleus*, within which is a minute structure known as a *nucleolus*. Surrounding the nucleus is a zone of less dense protoplasm known as *cytoplasm*. A delicate film, the *nuclear membrane*, separates the nucleoplasm (protoplasm of the nucleus) from the cytoplasm. Within the cytoplasm lies the *centrosome*. Surrounding the cytoplasm is a membrane known as the *cell membrane* and surrounding the cell membrane in certain vegetable cells and adherent to it is the *cell wall*.

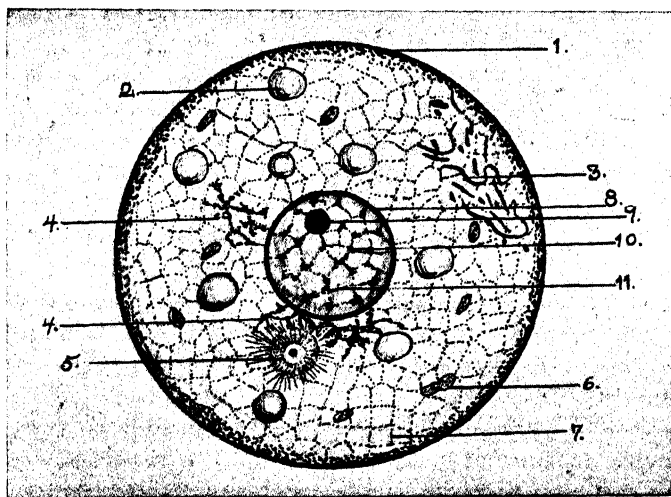


Fig. 19.—Diagram of a typical cell. 1, cell wall and cell membranes; 2, oil droplet; 3, chondriosomes; 4, granules; 5, centrosome; 6, vacuole; 7, fibrils of cytoplasm; 8, nuclear membrane; 9, nucleolus; 10, chromatin knot; 11, linin.

The *cell membrane* is a delicate film that limits the cytoplasm and presides over the exchange of food material and waste products between the cell and its surroundings. The cytoplasm is of a fluid, spongy fibrillar consistency and contains the cell sap, residual food material, and certain ex-

cretory products of the cell. In the unicellular organisms the cytoplasm is often divided into a clear outer portion (*ectoplasm*) and a more granular central portion (*endoplasm*). The *centrosome* is a minute deeply staining structure that plays an important part in cell division. In a general way it may be said that functions of the cytoplasm are: (1) aids in cell multiplication, (2) manufactures and stores food, (3) secretes enzymes which aid in the digestion of food, and (4) takes care of certain waste products.

The *nucleus* is usually a spherical body lying near the center of the cell, but in a general way its shape conforms to that of the cell. The framework of the nucleus is made up of a reticulum of rather coarse *linin fibrils* which is the essential living part of the nucleus. The reticulum is bathed by the nuclear sap, a fluid which furnishes the nucleus with food and water. On the fibers are located the *chromatin granules* (karyosomes) which unite to form chromosomes during mitosis. The number and size of the chromosomes depend on species, and are constant for each species. Chromatin is a most important part of the cell because it transmits the hereditary characteristics of the cell. In the absence of a nucleus the chromatin material is scattered throughout the cytoplasm. Granules of such material are known as *chromidia*. Within the nucleus are found one or more (usually one) nucleoli. The nucleolus takes an active part in the metabolism and multiplication of the cell and probably has a secretory function. In a general way we may say that the functions of the nucleus are: (1) rules over the growth and development of the cell, (2) controls the processes of oxidation that go on within the cell, (3) transfers the hereditary characteristics of the cell, and (4) controls reproduction.

All Typical Structures Not Present in Every Cell.—Most cells do not show all of the typical structure described above; for instance, animal cells do not have distinct cell walls, while bacteria and the mature red blood cells of man and many other animals do not have nuclei. In fact, the cytoplasm is the only structure that is common to all cells.

Definition of Cell.—Having described a cell we shall attempt to give a definition of it. Many definitions have been

proposed but none is perfect. The following is as good as we can devise. *A cell is a mass of protoplasm, usually microscopic in size, having a definite shape, performing a definite function, and having all the attributes of life.*

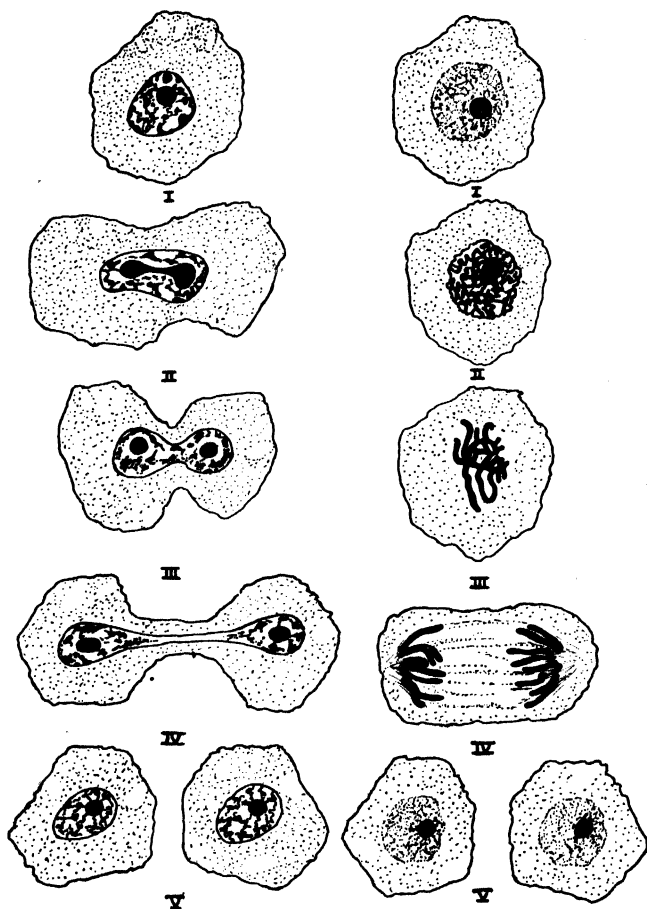


Fig. 20.—Comparative diagram showing various stages of amitosis (left) and mitosis (right). Note the elaborate nuclear changes and loss of nuclear membrane which occur in mitosis and the absence of such changes in amitosis.

Multiplication of Cells.—Every cell owes its existence to the division of a preexisting cell. Cells divide in two ways: (1) mitosis or indirect cell division; (2) amitosis or direct

cell division. In mitosis, division of the cell is preceded by a series of complicated nuclear and cytoplasmic changes. This type of division occurs characteristically in the higher animals and plants, but may be seen in the lower forms of life. In amitosis or direct cell division the cell divides without any remarkable preliminary cytoplasmic and nuclear changes. This form of division is rare in the higher animals and plants, but is common in the lower forms of life.

Unicellular Organisms: Nutrition, Circulation, Respiration, Excretion, and Response to Stimuli.—The biological processes of the higher forms of life are carried out by complicated organs and systems; for example, the circulatory and respiratory systems of the higher animals and the systems of translocation and transpiration in the higher plants. In the unicellular organism comparable processes are carried out within the confines of a single cell. Like the highly developed animal, the unicellular animal breaks down complex organic compounds and converts them into food materials. This is done within the protoplasmic substance of the cell. Some of the unicellular plants build up their food from simple compounds, while others obtain their food by oxidizing and breaking down complex organic compounds.

In the unicellular organism distribution of food within the cell is aided by currents in the cytoplasm. Respiratory exchange takes place by a process of osmosis through the cell membrane. Excretion is a function of the cell membrane and the fluid portion, of the cell. In some of the unicellular organisms a contractile vacuole plays an important excretory role.

Like the higher forms of life, unicellular organisms respond to external stimuli and some seem to be able to detect and approach food that they want and are repelled by things that are detrimental to them.

Locomotion of Unicellular Organisms.—For unicellular organisms to be motile they must be suspended in a liquid medium. Some move by extruding fingerlike processes. After the fingerlike processes are extruded, the body is pulled or flows in the direction in which the processes are extruded. This is known as *ameboid* motion. Others move

by means of protoplasmic extensions known as *flagella*. There may be a single flagellum, a tuft at one or both ends, or flagella may be generally distributed over the cell body. Other unicellular organisms move by means of delicate hair-like projections that surround the cell and move the cell along by lashing in unison. These projections are known as *cilia*. Organisms that move by means of flagella are known as *flagellates*. Those that move by means of cilia are known as *ciliates*.

Reproduction of Unicellular Organisms.—The reproductive system of the unicellular organism is rather simple. When it reproduces, it simply divides into two other organisms like itself. In some cases, however, there is a true sexual reproduction.

True-False Test

Place the word "true" or "false" before each statement.

- 1. Protoplasm forms the physical basis of all life.
- 2. Cells do not show any variation in size.
- 3. The micron is equivalent to 1/25,000 of an inch.
- 4. The average cell is about 7 μ in diameter.
- 5. The cell membrane is a delicate film that separates the nucleus from the cytoplasm.
- 6. The centrosome plays only a small part in cell division.
- 7. The shape of the nucleus in a general way conforms to that of the cell.
- 8. The number and size of chromosomes depend on the species.
- 9. Mature red blood cells in man have nuclei.
- 10. In mitosis or indirect cell division, very little change takes place in the nucleus.
- 11. The unicellular organism must be suspended in a liquid medium if locomotion is to take place.
- 12. Reproduction in the unicellular organisms is always of a true sexual nature.

Completion Test

1. Regardless of how complex or simple an organism may be, its unit of structure and function is the -----.
2. List the physical and chemical characteristics of protoplasm.
3. The ----- is a special unit of measurement which has been devised for the study of objects of microscopic size.
4. Cells, relative to shape, may be -----, -----, -----, or -----.

5. Draw a diagram showing the structure of the cell and label all parts.
6. The cell membrane presides over the exchange of food material and waste materials between the ----- and -----.
7. The residual food and cell sap are found in the -----.
8. Four functions of the cytoplasm are:
 - a. -----
 - b. -----
 - c. -----
 - d. -----
9. ----- is the most important part of the cell because it transmits the hereditary characteristics of the cell.
10. Four functions of the nucleus are:
 - a. -----
 - b. -----
 - c. -----
 - d. -----
11. The ----- is the only structure that is common to all cells.
12. Give the definition of a cell.
13. Two types of cell division are ----- and -----.
14. The type of cell division most often found is -----.
15. Explain how nutrition and elimination are carried out in the unicellular organism.
16. The means of locomotion of unicellular organisms are (explain each):
 - a. -----
 - b. -----
 - c. -----
17. How do bacteria divide?

References

- White, E. Grace: General Biology, St. Louis, 1946, The C. V. Mosby Co.
Potter, George E.: Textbook of Zoology, St. Louis, 1947, The C. V. Mosby Co.
Beaver, William C.: Fundamentals of Biology, St. Louis, 1946, The C. V. Mosby Co.
Hoskins, Margaret M., and Bevelander, Gerrit: Essentials of Histology, St. Louis, 1945, The C. V. Mosby Co.
Jordan, Harvey Ernest: A Textbook of Histology, New York, 1945, D. Appleton-Century Co.

CHAPTER V

GENERAL CHARACTERISTICS OF BACTERIA

Definition.—*Bacteria* (sing. *bacterium*) are very minute unicellular organisms that do not contain chlorophyl or organized nuclei and usually divide by simple transverse division. Bacteria are usually classed as members of the plant kingdom, but they differ from the higher plants in that they do not contain chlorophyl and some are motile. Bacteria represent the lowest form of life, being more simple in structure and mode of development than either the molds or yeasts. Although this is true, they have an elaborate and complicated life history.

Distribution and Importance.—Bacteria are widely distributed in nature. They are found within and upon our bodies, in the food we eat, the water we drink, and the air we breathe. They are plentiful in the upper layers of the soil, and no place on earth except possibly the peaks of snow-capped mountains are free from them. Our skins have a plentiful bacterial population, and bacteria make up a large portion of the contents of our intestinal tract. There are about two thousand species of bacteria; of this number about one hundred species produce disease in man. Some of the bacteria that produce disease in man also produce disease in the lower animals. Other bacteria produce disease in the lower animals only and still others attack only plants. The majority, however, do not attack man, lower animal, or living plant, and either do not affect them at all or are helpful to them. In fact, if the activities of bacteria were to cease, all plant and animal life would soon become extinct. Bacteria that cause disease are spoken of as *pathogenic*; those that do not cause disease are spoken of as *nonpathogenic* bacteria.

Chemical Composition of Bacteria.—The bacterial cell is composed of water, proteins, fats, carbohydrates and related substances, and various inorganic components, such as sulphur and salts of potassium, iron, etc., i.e., those elements

that make up protoplasm. While there is considerable variation in different species, on an average from 80 to 90 per cent of the bacterial cell is made up of water; proteins compose less than 1 per cent. Each species has a type of protein peculiar to itself.

Shape and Arrangement of Bacteria.—Bacteria occur in three basic shapes, namely:

1. Spherical ----- *coccus**
2. Rod shaped ----- *bacterium* or *bacillus*
3. Spiral shaped ----- *vibrio*, *spirillum*, *spirochete*

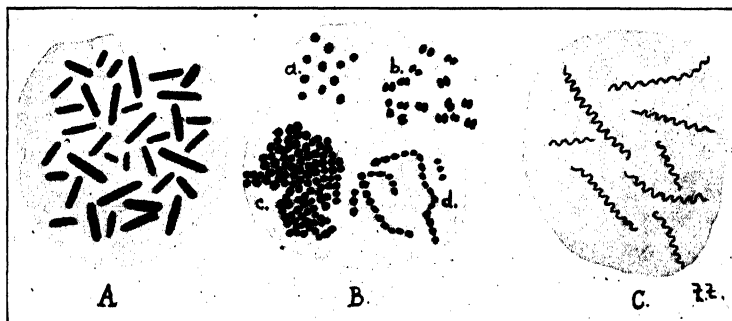


Fig. 21.—The three shapes of bacteria. A, Bacilli; B, cocci (a, micrococci; b, diplococci; c, staphylococci; d, streptococci); C, spirilla.

When one of these terms occurs as a part of the name of an organism, the shape of the organism is indicated; for instance the term *B. anthracis* indicates the rod-shaped bacterium that causes anthrax (B. is an abbreviation for bacillus), while the term “gonococcus” indicates the spherical bacterium that causes gonorrhea. A *vibrio* is a curved organism which has a commalike shape. A *spirillum* is a spiral organism whose long axis remains rigid when the organism is in motion. A *spirochete* is a spiral organism whose long axis bends when the organism is in motion.

*The student sometimes fails to differentiate the singular and plural forms of certain common words used in bacteriological discussions. The following are a few of them:

Singular
Coccus
Bacillus
Spirillum
Bacterium
Medium

Plural
Cocci
Bacilli
Spirilla
Bacteria
Media

Cocci are often not perfectly round but may be elongated, oval, flattened on one side, etc. Some bacilli are long and slender. Others are so short and plump that they may be mistaken for cocci. The ends of bacilli are usually rounded but may be square or concave.

When bacteria, especially cocci, divide, the manner in which they divide and their tendency to cling together often give them a characteristic arrangement. Cocci that divide in such a manner as to form pairs are known as *diplococci*. The opposing sides of diplococci are often flattened (examples—gonococci and meningococci). Cocci that divide and cling end to end to form chains are known as *streptococci*. Those that divide in an irregular manner to form grapelike clusters or broad sheets are known as *staphylococci*.

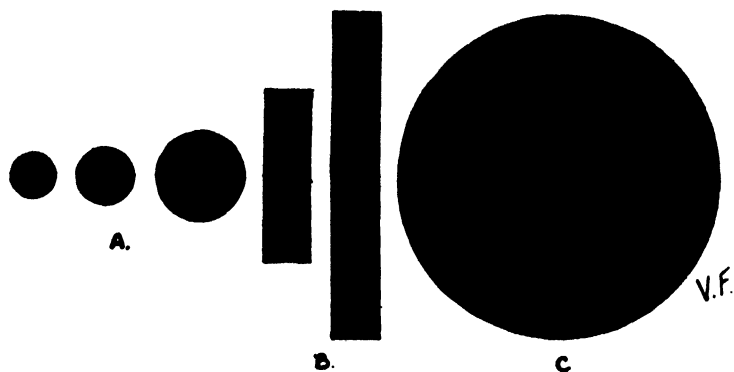


Fig. 22.—Diagram showing relative size of bacteria and red blood cell. A, various cocci; B, bacilli; C, red blood cell. (Modified from Lutman: *Microbiology*. McGraw-Hill Book Co.)

Cocci that divide and separate at once to occur as single organisms are known as *micrococci*. Other characteristic arrangements of cocci are in groups of four (tetrads) and packets of eight (sarcinae). No pathogenic cocci are found in the latter group. Bacilli that occur in pairs are known as *diplobacilli* and those that occur in chains are known as *streptobacilli*. The diplobacillus and streptobacillus arrangements are not common.

Size of Bacteria.—Cocci range from 0.15 to 2 μ in diameter with an average of 0.8 to 1.2 μ . The smallest bacillus is about 0.5 μ in length and 0.2 μ in diameter. The largest

pathogenic bacilli are seldom greater than $1\ \mu$ in diameter and $3\ \mu$ in length, while the average diameter and length of pathogenic bacilli are 0.5 and $2\ \mu$ respectively. Non-pathogenic bacilli may be much larger, reaching a diameter of $4\ \mu$ and a length of $20\ \mu$. The spirilla are usually narrow organisms and are from 1 to 14 microns in length. Different species of bacteria show marked variation in size, and there is some variation within a species but, as a rule, the size of each species is fairly constant.

Structure of Bacteria.—As has been said before, bacteria are always unicellular. They are so tiny and transparent and are so slightly refractile that they are difficult to see unless rendered visible by staining. Their bodies are homogeneous or slightly granular. Their shape is maintained by a cell membrane which is so delicate that it cannot be seen with the ordinary microscope. Bacteria do not contain definite nuclei, but nuclear material is scattered throughout the cell and has some tendency to be more dense near the center of the cell. As revealed by the electron microscope, each bacterium has a well-defined cell wall and contains spherules and granules of various types. It has been suggested that certain granules seen with the electron microscope are true nuclei. This remains yet to be proved or disproved.

Surrounding many bacteria is a gelatinous envelope or *capsule*. It is indistinct in most bacteria but is well developed in a few (example—the pneumococcus, Welch's bacillus, and *B. mucosus capsulatus*). Capsule formation is most prominent in organisms taken directly from the animal body, and when grown on artificial media these organisms often lose their ability to form capsules. Capsules do not stain with the ordinary bacteriological dyes and appear as a clear halo around the bacterium. In some cases the capsule is two or three times as broad as the bacterium that it surrounds. They may, however, be stained by special methods. Although a capsule has not been demonstrated in many species of bacteria, it is probable that an essentially similar structural modification exists in all of them. The presence of a capsule appears to increase the virulence of an organism by protecting it against phagocytosis.

Within some bacteria (example—*C. diphtheriae*) are seen granules that stain more deeply than the remainder of the cell. These granules are known as *metachromatic granules*. In some species they are arranged irregularly within the cell, while in others they are located in one or both ends of the cell. When occurring at the ends of the cell they are

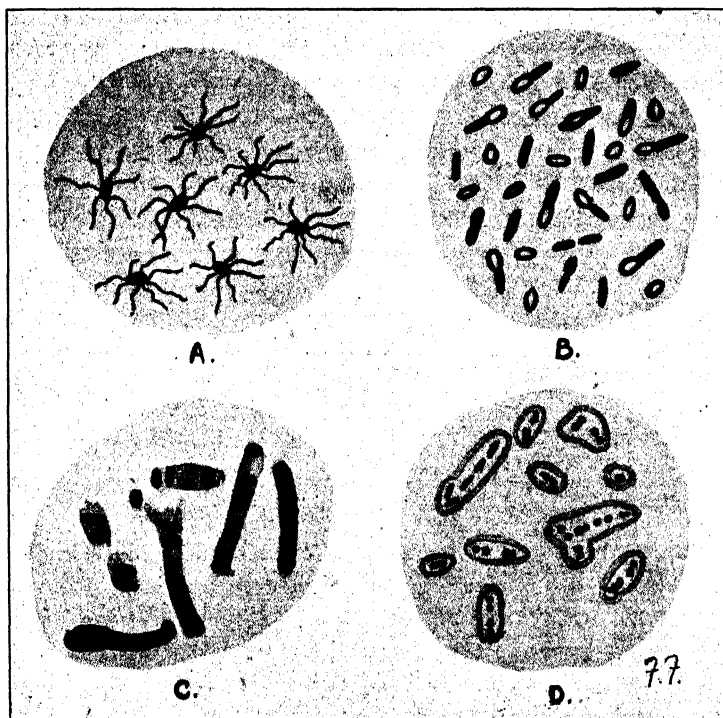


Fig. 23.—Drawing of bacteria showing flagella, spores, metachromatic granules and capsules. A, flagella; B, spores; C, metachromatic granules; D, capsules.

known as *polar bodies*. According to some investigators metachromatic granules represent remnants of nuclear material, but most observers believe that their true nature is yet unknown. Some think that they are reserve food material.

Motility.—Many bacilli and all spirilla are motile when suspended in a suitable liquid. True motility has not been

observed in cocci. The organs of bacterial locomotion are fine hairlike appendages known as *flagella* that spring from the bacterial cell and cause it to move along by their lashing. A bacterium may have one, a few, or many flagella, and the flagella may be attached to one end, both ends, or all around the organism. Some spirochetes have a flexible form which aids the action of their flagella by a sinuous motion of the entire cell. Flagella do not stain with the ordinary bacteriological stains but may be stained by special methods.

True motility in which the organism changes its position in relation to its neighbors should not be mistaken for Brownian motion, a peculiar dancing motion possessed by all finely divided particles suspended in a liquid.

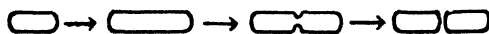


Fig. 24.—Diagrammatic illustration of the multiplication of bacteria. Note in succession: "young" bacterium, "full grown" bacterium, dividing bacterium, and two "young" bacteria. This process of multiplication is known as fission or simple transverse division. (From Burdon: *A Text-book of Bacteriology*. By permission of The Macmillan Co., publishers.)

Reproduction.—The typical mode of bacterial reproduction is by simple transverse division (fission) in which the cell reaches its maximum size and becomes constricted in the middle after which the constriction deepens and separates the organisms into halves. Each part soon reaches its full size and divides. The line of division is across the long axis of the organism. For a "newborn" bacterium to reach adult size and divide requires from fifteen to thirty minutes. Reproduction is always specific; i.e., staphylococci always produce staphylococci, *Corynebacterium diphtheriae* always produce *Corynebacterium diphtheriae*, etc.

Spore Formation.—When gradually subjected to influences unsuitable for bacterial growth, such as lack of food or water or unsuitable temperatures, many species of bacteria die; but some form, within their cytoplasm, bodies with increased capabilities of withstanding influences adverse to bacterial growth. These bodies are known as *spores*. When conditions suitable for bacterial growth are again established the spore converts itself back into the original actively multi-

plying bacterial form (germinates). Spore formation seems to be a characteristic of bacilli only. Of the bacilli not more than one hundred and fifty species form spores. Of these most are saprophytic. The important pathogenic spore-forming bacteria are those that cause tetanus, gas gangrene, and anthrax. Botulism is due to the toxins produced by a spore-bearing organism, but the organism itself does not invade the body. Recent studies indicate that spore formation is not necessarily the result of deleterious circumstances but may occur in certain cases as a normal growth phenomenon.

Spores are formed as follows: The bacterial cell forms within its substance a round or oval highly refractile body surrounded by a capsule. This body increases in size until it is as broad or broader than the cell and about one-half as long. The portion of the cell that remains gradually disintegrates leaving only the spore. Spore formation is not a reproductive but a protective phenomenon because a single bacterium forms but one spore and a spore forms only one bacterium. Bacteria which do not form spores and spore-bearing bacteria in which spores are not forming at the time are known as *vegetative* bacteria. Those in which spores are forming are known as *sporulating* bacteria, and spores from which the remainder of the cell has disappeared are known as *free* spores.

Spores do not stain with the ordinary bacteriological stains but may be stained by special methods. Ordinary stains of sporulating organisms show the spores as clear unstained areas which may be situated in the ends of the bacteria or near their centers. In some cases the spore is broader than the remainder of the bacterial cell. This causes the bacterium to assume a spindle shape if the spore is situated near the middle and a club shape if it is situated at or near the end of the cell. The shape and position of their spores are of considerable value in identifying certain species of bacteria.

Spores are especially resistant to heat, chemicals, and drying, but the vegetative forms of spore-bearing bacteria are no more resistant to these or other adverse influences than

nonspore-bearing bacteria. An idea of the protective value of spores may be drawn by saying that some spores withstand boiling for hours, while a temperature less than boiling will kill all vegetative bacteria within ten to fifteen minutes. They have also been known to resist the temperature of liquid air (-140° C.) for six months. Their resistance is probably due to the membrane about them and the concentrated, water free nature of their material. While only a few species of bacteria produce spores, they are of great importance because their spores are universally present, which makes it necessary to use spore-killing methods in bacteriological and surgical sterilization and in the canning industry.

Classification of Bacteria.—The classification of bacteria is a difficult problem. This applies to both the separation of bacteria into groups and the placing of certain organisms in their proper group. Shape is probably the most important factor in the general classification of bacteria, but other characteristics, such as cultural behavior, antigenic properties and pathogenicity, must be considered. The following classification is widely used:

1. *Cocci*—spherical or elliptical cells.
2. *Spirilla*—cells curved or spiral shaped.
3. *Bacteria*—cells rod-shaped, without spores.
4. *Bacilli*—rod-shaped, with spores.
5. *Mycobacteria*—the acid-fast bacteria and certain others.
6. *Spirochetes*.

In addition to the classification given above, bacteria may be divided into comparatively large groups from any of the following standpoints:

1. Food Requirements:

- (1) Saprophytes—grow on dead organic matter.
- (2) Parasites—grow on living matter.

2. Oxygen Requirements:

- (1) Aerobes—grow only in the presence of free oxygen.
- (2) Anaerobes—grow only in the absence of free oxygen.

3. Disease Production:

- (1) Pathogenic—those that produce disease.
- (2) Nonpathogenic—those that do not produce disease.

4. Motility:

- (1) Motile.
- (2) Nonmotile.

5. Formation of Spores:

- (1) Spore formers.
- (2) Nonspore formers.

6. Capsule Formation:

- (1) Encapsulated.
- (2) Nonencapsulated.

7. Toxin Production:

- (1) Produce extracellular toxins.
- (2) Produce endotoxins.

8. Staining Reactions:

- (1) Reaction to acid-fast stains
 - a. acid-fast.
 - b. nonacid-fast.
- (2) Reaction to Gram's stain
 - a. Gram-positive.
 - b. Gram-negative.

9. Cultural Characteristics:

- (1) Grow on simple media.
- (2) Grow only on special media.
- (3) Will not grow on any artificial medium.

The preceding classifications are in no way comparable to some of the complete classifications found in books on advanced bacteriology. They are, however, based on important characteristics and are of value in identifying bacteria. In addition, the terms used are ones that the nurse will often hear and should understand.

Bacterial Variation.—Bacteria of the same species growing under different or identical conditions are not necessarily exactly alike. This deviation from the parent form is known as *variation*. Variation may affect the size, shape, chemical composition, colony characteristics, or biological action of bacteria and may be temporary or permanent. Variation may be caused by some external influence, such as kind of culture medium, temperature of growth, length of time grown artificially, or it may be due to factors inherent in the bacteria themselves. In the remainder of this discussion

no attempt will be made to give the underlying causes of bacterial variation but a few examples will be given.

Bacteria belonging to the same species and growing under most favorable conditions may show considerable variation in size, shape, and appearance. This is known as *pleomorphism*. The members of some species assume irregular and bizarre shapes, stain irregularly, become swollen, shrunken, or granular when grown under unfavorable conditions (ex. old cultures). These are known as *involution forms*.

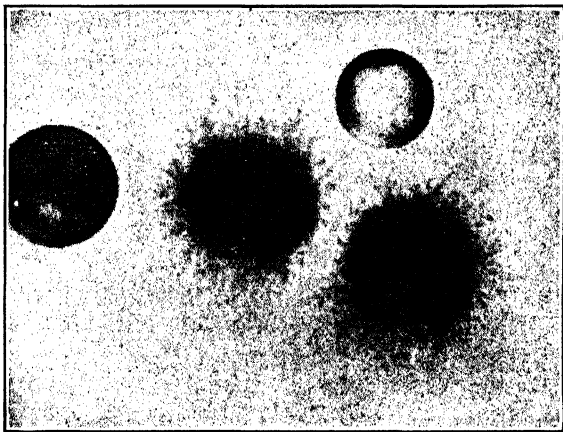


Fig. 25.—Smooth and rough colony types. (Courtesy of F. E. Collen.) (From Eisenberg and Huntly: *Principles of Bacteriology*. The C. V. Mosby Co.)

When a colony of a pure culture of an organism is streaked over the surface of a culture medium, the resultant colonies may have entirely different characteristics. At one extreme are the smooth or S-type colonies which are regular in outline, round, moist, and glistening. At the other extreme are the rough or R-type colonies which are larger, irregular in outline, indented, and wrinkled. Between the two there are intermediate forms. By proper laboratory manipulation organisms forming S-type colonies may be so changed that they form R-type colonies and vice versa. Organisms forming S-type colonies are usually more highly virulent and promote greater formation of antibodies than organisms forming R-type colonies. These facts are of im-

portance in both immunology and epidemiology. It explains why some vaccines for a given disease, for instance typhoid fever, have more protective power than others; i.e., vaccines made from typhoid bacilli forming S-type colonies bring about a high degree of immunity while those made from typhoid bacilli forming R-type colonies bring about a slight degree of immunity. These variations also offer some explanations of the rise and fall of epidemics.

Among other examples of bacterial variation the following may be cited. By certain laboratory manipulations organisms that are ordinarily motile may be made to grow in a nonmotile form. Organisms that are surrounded by a capsule when growing in the animal body often lose their capsule when grown on artificial media. In some cases capsule formation may be restored by injection into a susceptible animal. When anthrax bacilli, which normally form spores, are grown at a high temperature a race of anthrax bacilli that have permanently lost their ability to form spores develops. One variety of colon bacillus when grown on certain lactose media dissociates into strains that ferment lactose and those that do not. Upon further cultivation the lactose-fermenting strain continues to produce lactose fermenters, while the strain that does not produce lactose will again dissociate into lactose fermenters and nonlactose fermenters. Under certain laboratory conditions organisms that are ordinarily nonpathogenic may be made to take on pathogenic properties, while those that are ordinarily highly pathogenic may be rendered temporarily or permanently nonpathogenic.

Adaptability of Bacteria.—One of the characteristic attributes of living cells is their power to adapt themselves to their surroundings. This is probably more true of bacterial cells than many other types of cells. For instance, certain bacteria which require specially prepared media to sustain their continued growth when first isolated from the animal body gradually acquire the ability to grow on media that are devoid of the growth promoting and enriching materials found in the media necessary to sustain their early growth. Not only this, but they may be grown artificially

in a gradually changing environment until at last they are able to grow under conditions of food supply, temperature, moisture and oxygen supply far different from the ones in which they originally grew best. This characteristic which enables bacteria to adapt themselves to their environment helps to preserve them through the changes in food supply, moisture, temperature, etc., to which Nature subjects them.

Drug Fastness.—An adaptation which has considerable therapeutic importance is the acquisition by an organism of an increased resistance to a drug. This is of special importance in therapy with the sulfonamide drugs and with penicillin because in each case several strains of certain bacteria have acquired resistance to the drug being used. For instance, certain strains of gonococci have become refractory to the action of the sulfonamide drugs and certain strains of pneumococci have acquired a resistance to penicillin. An organism which acquires this resistance toward a drug used in the treatment of a disease is said to be “drug fast.” The fact that a given organism is resistant to one of the sulfonamide drugs in no way indicates that the organism is resistant to penicillin, and resistance to penicillin in no way indicates resistance to the sulfonamide drugs.

True-False Test

Place the word “true” or “false” before each statement.

- 1. All bacteria are nonmotile.
- 2. *B. anthracis* is a spiral-shaped bacterium.
- 3. Cocci are always perfectly round.
- 4. The ends of bacilli are usually round but may be square or concave.
- 5. Coccus is the singular form of the term cocci.
- 6. Spirillus is the singular form of the term spirilla.
- 7. Bacteria are usually classified as members of the animal kingdom.
- 8. A large portion of the contents of the intestinal tract is made up of bacteria.
- 9. Bacteria must be stained to make them visible because of their transparency.
- 10. Spore formation seems to be a characteristic of bacilli only.
- 11. Spores may be destroyed easily by boiling.
- 12. Bacteria are probably more capable of adapting themselves to their surrounding than any other type of cell.

Completion Test

1. Bacteria are unicellular organisms that do not contain -----
----- and divide by ----- division.
2. Bacteria that cause disease are spoken of as -----
and those that do not cause disease, as -----.
3. Bacteria occur in three basic shapes; namely, -----,
-----, and -----.
4. Cocci that divide in such a manner as to form pairs are known as
-----; examples of these organisms are
----- and -----.
5. The organisms of bacterial locomotion are fine hairlike appendages
known as -----.
6. The typical mode of bacterial reproduction is by -----
-----.
7. (a) When gradually subjected to unsuitable influences for bacterial
growth, some bacteria form bodies with increased capabilities of
withstanding these influences. These bodies are known as -----
-----.
- (b) Some of the most important of the organisms capable of form-
ing these bodies are -----,
and -----.
8. (a) Saprophytes are organisms which grow on -----
organic matter.
- (b) Parasites are organisms which grow on -----
organic matter.
9. (a) ----- grow only in the presence of oxygen.
- (b) ----- grow only in the absence of oxygen.
10. Classify organisms according to staining reaction.

References

- Zinsser and Bayne-Jones: A Textbook of Bacteriology, New York, 1939, D. Appleton-Century Co.
- Jordan, Edwin O., and Burrows, William: Textbook of Bacteriology, Philadelphia, 1945, W. B. Saunders Co.
- Burdon, Kenneth L.: A Textbook of Bacteriology, New York, 1947, The Macmillan Co.
- Stitt, Clough, and Branham: Practical Bacteriology, Haematology and Parasitology, Philadelphia, 1948, P. Blakiston's Son and Company.
- Topley and Wilson: Principles of Bacteriology and Immunology, Baltimore, 1946, Williams & Wilkins Co.

CHAPTER VI

CONDITIONS AFFECTING THE GROWTH OF BACTERIA

For bacteria to multiply most rapidly certain requirements must be met: (1) sufficient food of the proper kind must be present, (2) moisture must be available, (3) the temperature must be that most suitable for the species, (4) the proper degree of alkalinity or acidity must be present, (5) the oxygen requirements of the species must be met, (6) light must be partially or completely excluded, and (7) there must not be too great an accumulation of the products of bacterial growth. Any great departure from any of these requirements will greatly modify bacterial growth.

Food.—Organisms that obtain their nourishment from nonliving organic material are known as *saprophytes*. Those that depend on living matter for their nourishment are known as *parasites*. *Facultative saprophytes* usually obtain their nourishment from living matter but may obtain it from dead organic matter. *Facultative parasites* usually obtain their nourishment from dead organic matter but may obtain it from living matter. *Strict parasites* are organisms that thrive on living matter only. *Strict saprophytes* are organisms that thrive on dead organic matter only. Some of the pathogenic bacteria are strict parasites; many are facultative saprophytes and a few are facultative parasites (ex. bacteria that cause tetanus and those that cause gas gangrene). The organism on which a parasite lives is known as a *host*. Regardless of whether bacteria are saprophytes or parasites, they require carbon, oxygen, nitrogen, hydrogen, and certain mineral salts for their nourishment. The most important of the mineral salts are those of calcium, magnesium, potassium, and sodium. With the exception of a few saprophytic species all bacteria derive their carbon and nitrogen from organic materials, parasites deriving theirs from living organic material and saprophytes deriving theirs from dead organic material. A few species re-

quire vitamin-like substances for their growth. Organisms which obtain their nourishment by breaking down organic matter are known as *heterotrophic organisms*. Those that obtain their food by building up inorganic substances are known as *autotrophic*. All pathogenic bacteria are heterotrophic.

Food materials prepared for the growth of bacteria in the laboratory are known as *culture media*. Some bacteria will grow on practically any properly prepared culture medium. Others grow only on specially nutritious media and a few will not grow on any medium. Many bacteria require vitamins or, at least, vitamin-like substances for their nourishment. The character of the medium required to support the growth of an organism is one of the important characteristics which the bacteriologist uses in the identification of that organism.

Moisture.—Water is necessary for the growth of bacteria because they cannot absorb food material unless it is in solution. Drying is highly detrimental to bacterial growth. Delicate bacteria like the gonococcus resist drying for only a few hours and highly resistant bacteria like the tubercle bacillus succumb to drying within a few days. Spores, however, may resist drying for years. As a rule, bacteria which have capsules are more resistant to drying than those that have not. Cleaning walls and floors by scrubbing and the destruction of bacteria by natural drying have to a great degree replaced fumigation in the control of communicable diseases.

Temperature.—For each species of bacteria there is a minimum, optimum, and maximum temperature meaning respectively the lowest temperature at which the species will grow, the temperature at which it grows best, and the highest temperature at which it will grow. The optimum temperature for a species corresponds to the average temperature of its usual habitat. For instance, bacteria that naturally live in or attack the human body live best at 37.5° C. (the normal temperature of the body). The lowest temperature at which any of these species will continue to multiply is about 20° C. and the highest is from 42°-45° C., but

many of them will not grow at a temperature more than a few degrees above or below the optimum. The majority of saprophytic bacteria grow best between 25° and 30° C., but some may grow at a temperature as high as 60° C. A few species grow at temperatures little above the freezing point.

Cold retards or stops bacterial growth, but when the bacteria are later exposed to a temperature favorable for their growth, multiplication will be resumed. Refrigeration is one of the best methods of preserving bacterial cultures. Actual freezing, however, is rather destructive to bacteria.

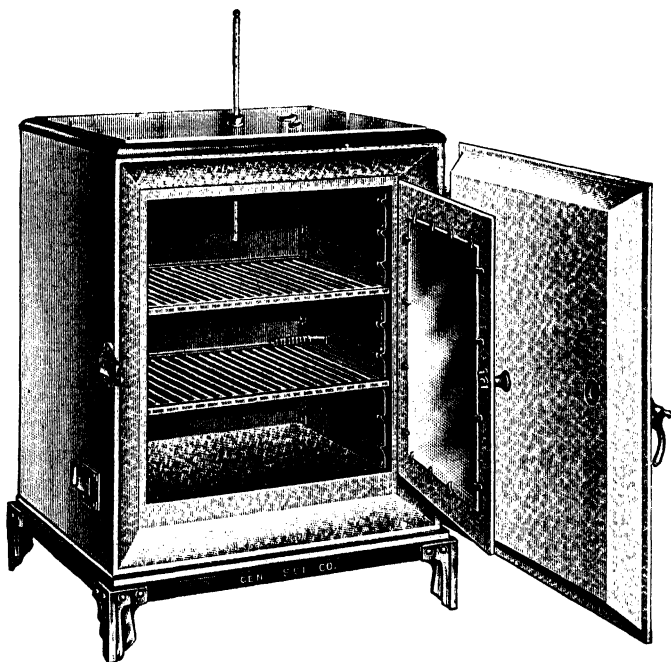


Fig. 26.—A bacteriological incubator. This incubator is heated by electricity and the temperature is maintained at a constant level by the steel spiral (thermostat) seen above the first shelf. (Courtesy of Central Scientific Co.)

High temperatures are much more injurious to bacteria than low ones. All nonspore-bearing disease-producing bacteria and most nonspore-bearing nonpathogenic bacteria are killed when exposed in watery liquids to a temperature of 60° C. for thirty minutes. This is the basis of the process

of pasteurization. Staphylococci are the most resistant of all nonspore-bearing pathogenic bacteria.

No vegetative organism except possibly certain species of staphylococci can withstand boiling for even a few minutes, but certain spores may resist boiling for hours. A dry temperature of 120°-130° C. kills all vegetative bacteria within an hour and a half and one of 150° C. kills all spores within an hour. A moist temperature of 120° C. kills all vegetative bacteria and spores within fifteen to twenty minutes.

Reaction.—For each species of bacteria there is a certain degree of alkalinity or acidity at which growth is most rapid. Most pathogenic bacteria grow best in a neutral or slightly alkaline medium. The reaction of culture media is carefully adjusted so that the degree of alkalinity or acidity will be most suitable for the bacteria that are to be cultivated.

Oxygen.—Organisms that grow in the presence of free oxygen are known as *aerobes*. Those that cannot grow in the presence of free oxygen but obtain their oxygen from oxygen-containing compounds are known as *anaerobes*. Organisms that live best in the presence of free oxygen but may live in its absence are known as *facultative anaerobes*. Those that live best in the absence of free oxygen, but may live in its presence are known as *facultative aerobes*. Organisms that cannot develop at all in the absence of free oxygen and those that cannot develop at all in its presence are known as *obligate aerobes* and *obligate anaerobes* respectively. Few of the pathogenic organisms are anaerobic. Of these the organisms of tetanus and malignant edema are most important. Organisms which do not grow in the complete absence of oxygen but grow best in an amount of oxygen less than that contained in the air are known as *micro-aerophiles*.

Light.—Most bacteria are injured by diffuse daylight and are killed within a few hours by direct sunlight. Bright daylight has an effect similar to that of sunlight, but it is not so marked. Violet, ultraviolet, and blue lights are highly destructive to bacteria; green light is much less so, while red

and yellow light have little bactericidal action. Some operating rooms are equipped with units that distribute ultraviolet light throughout the room. This appears to reduce greatly the incidence of infections at the time of operation. Ultraviolet light also has been found to reduce the incidence of infections in children's wards, barracks, and other places where people live in rather close contact.

Products of Bacterial Growth.—Bacterial reproduction is so rapid that the bacteria soon exhaust their food supply and give rise to products that inhibit further bacterial growth. Important among these products are acids that inhibit growth by changing the reaction of the medium. A practical application of the prevention of the growth of bacteria by acids is found in the pickling industry. If it were not for these inhibitory influences bacteria would soon completely submerge the whole world because it is estimated that with unrestricted growth a single bacterium would have a progeny of 280 trillion at the end of twenty-four hours.

Electricity.—Within itself electricity does not destroy bacteria, but it causes heat and changes in the medium in which the bacteria are growing that may kill them. The electric light inhibits bacterial growth, but the inhibition is an effect of light instead of electricity. X-ray has little effect on bacteria but radium retards their growth.

Chemicals.—Certain chemicals destroy, others inhibit, the growth of bacteria. These will be considered later. Some substances attract bacteria while others repel them. The former condition is called *positive chemotaxis* and the latter *negative chemotaxis*.

Osmosis.—The cell membranes of bacteria, like those of other living cells, act as semipermeable membranes, and when bacteria are suspended in a liquid containing less dissolved substance than the bacterial protoplasm, water passes into the bodies of the bacteria, causing them to swell and possibly to burst (plasmolysis). When suspended in a liquid containing more dissolved substances than the bacterial protoplasm, water passes out of the bodies of the bac-

teria and the bacteria shrink and die (plasmolysis). This is taken advantage of in preserving fruits with strong sugar solutions and meats with brine. Plasmolysis is a poor term, because lysis indicates dissolution of cells, which does not occur in plasmolysis.

Shaking.—Prolonged shaking will destroy many bacteria.

Pressure.—Marked pressure over a long period of time will either inhibit the growth of bacteria or destroy them.

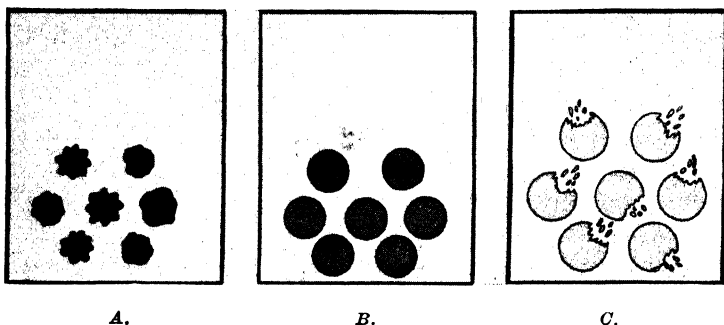


Fig. 27.—Diagrammatic representation of what happens to a bacterium or other cell when it is suspended in a liquid containing more, an equal amount of, and less, dissolved substance than is present in the protoplasm of the cell. *A*, Liquid containing more dissolved substance than the cell protoplasm; water passes from the cell to the surrounding fluid and the cell shrinks. *B*, Liquid and cell protoplasm contain the same amount of dissolved substance; no transfer of water, no change in cell. *C*, Liquid contains less dissolved substance than cell protoplasm; water passes from liquid into the cell, causing it to swell and burst.

Symbiosis and Antagonism.—Certain species of bacteria grow better in the presence of certain other species and such associated species are able to accomplish harmful or beneficial results that neither species is able to accomplish alone. For instance, pneumococci and influenza bacilli multiply more rapidly when grown together than when either is grown alone, and certain organisms when grown together in a culture will produce fermentation while either grown alone will not. This is known as *symbiosis*. *Commensalism* is the term applied when two organisms live together to the advantage of one without injury to the other. In some cases the presence of certain species inhibits the growth of others. For instance, growth of the gonococcus is inhibited by the presence of almost any other species of bacteria. This is

known as *antagonism*. Some of the theories put forth to explain antagonism are: (1) one organism secretes an enzyme or toxic substance that prevents the growth of the other, and (2) in the body, one organism acts on the body cells and promotes a defense mechanism against the other. The latter theory has been used to explain the treatment of paresis with malaria.

True-False Test

Place the word "true" or "false" before the following statements.

- 1. Saprophytes do not require any oxygen.
- 2. Food materials prepared for growth of bacteria in the laboratory are known as culture media.
- 3. Facultative saprophytes usually obtain their nourishment from living matter but may obtain it from dead organic matter.
- 4. Facultative parasites may obtain their food from living matter.
- 5. The majority of bacteria are strict saprophytes.
- 6. Some bacteria will grow on practically any properly prepared culture medium.
- 7. The type of culture medium supporting growth of an organism cannot be used to identify the organism.
- 8. The optimum temperature for a species corresponds to the average temperature of its usual habitat.
- 9. If the growth of bacteria has been retarded and later the bacteria are exposed to temperature favorable for their growth, multiplication will not be resumed.
- 10. Freezing is destructive to bacteria.
- 11. High temperatures are much more injurious to bacteria than low ones.
- 12. No bacteria will ever resist boiling for hours.
- 13. Most pathogenic bacteria grow best in a neutral or slightly alkaline medium.
- 14. Facultative aerobes grow best in presence of free oxygen but may grow in the absence of oxygen.
- 15. Most bacteria are not killed by direct sunlight.
- 16. Bacterial reproduction may be so rapid that the food supply may become exhausted.
- 17. It is never practical to use ultraviolet light while doing surgery to prevent infection.
- 18. Within itself electricity does not destroy bacteria.
- 19. Plasmolysis of bacteria is the shrinking of the cell due to the passing of water out of the bodies of the bacteria because of the more concentrated surrounding medium.

Completion Test

1. List seven requirements for rapid bacterial growth.
2. Organisms that depend on living matter for their nourishment are known as _____.
3. Organisms that depend on nonliving organic material for nourishment are known as _____.
4. Bacteria like the _____ resist drying for only a few hours. _____ will resist drying for years.
5. Bacteria that normally attack the human body live best at what degree of temperature? _____ to _____° C.
6. What is the minimum temperature for most pathogenic bacteria? _____° C.
7. What is the maximum temperature for such bacteria as above? _____° C.
8. What is the basis of the process of pasteurization?
9. Organisms that grow in the presence of free oxygen are known as _____.
10. Organisms that cannot grow in the presence of free oxygen are known as _____, and an example of this is the _____.
11. The condition in which chemical substances attract bacteria is known as _____.
12. Define symbiosis and antagonism. Also give examples of each.
13. Give two theories that are offered as an explanation of antagonism.

References

- Zinsser and Bayne-Jones: Textbook of Bacteriology, New York, 1939, D. Appleton-Century Co.
- Jordan, Edwin O., and Burrows, Williams: Textbook of Bacteriology. Philadelphia, 1945, W. B. Saunders Co.
- Topley and Wilson: Principles of Bacteriology and Immunology, Baltimore, 1946, Williams & Wilkins Co.

CHAPTER VII

SPECIAL ACTIVITIES OF BACTERIA

There are certain special bacterial activities which are to a great extent responsible for the changes that the bacteria bring about. The three most important of these are: (1) the production of enzymes; (2) the processes of denitrification, nitrogen fixation, and nitrification; and (3) the production of toxins. Less important are: (1) pigment production, (2) heat production, (3) light production, and (4) the production of odors. Most of these special activities have for their primary purpose the nutrition of the bacteria. Few of them are possessed by all bacteria.

Production of Enzymes; Putrefaction; Fermentation.—Enzymes are substances produced by living cells that are capable of bringing about chemical changes without undergoing any change themselves. All cells probably produce some form of enzyme. Cells of the higher animals that are especially well known on account of their enzyme production are the cells of the salivary glands (produce ptyalin), the cells of the stomach glands (produce pepsin and rennin), and the cells of the pancreas (produce trypsin, etc.). Bacteria produce enzymes that are remarkably like those produced by the organs of the higher animals. The primary purpose of bacterial enzymes is to break complex food materials down into simple materials fit for assimilation by the bacteria.

The word "enzyme" is of Greek origin and means "in yeast" (*en*, in; *zyme*, yeast). Enzymes are protein in nature or are in some way joined to proteins. Some contain nitrogen; a few have been crystallized. They are best recognized by their action. They have some rather striking characteristics. Their activity is not lessened when they are separated from the cells that produced them. Very small amounts of enzyme are capable of bringing about most extensive chemical changes. They are not destroyed during the change, but their activity may be inhibited by the products of the re-

action. Enzymes bear a close resemblance to the catalytic agents of inorganic chemistry. Their action is specific; i.e., each enzyme causes its own peculiar type of chemical change and that kind only.

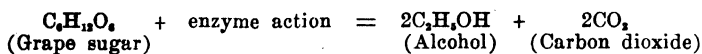
Enzymes are most active at a temperature of from 35° to 40° C. A temperature of 60° C. destroys them within ten to thirty minutes. Freezing retards their action but does not destroy them. A medium that is too acid or too alkaline inhibits their action or destroys them. Bacterial enzymes are often more resistant to disinfectants than the bacteria that produced them.

From the standpoint of cell relation enzymes may be classified as *ectoenzymes* and *endoenzymes*. The former are formed within the cell and are diffused through the cell membrane into the surrounding medium. Endoenzymes are liberated only by the disintegration of the cells that produce them. Ectoenzymes are much more important. From the standpoint of action bacterial enzymes may be classified as protein splitting, sugar splitting, and fat splitting. Enzymes are named by adding the suffix *ase* to the name of the substances upon which they act or to the name of the type of reaction that they produce. For instance, enzymes that act on carbohydrates are called *carbohydrases* and those which bring about reduction are called *reductases*.

The proteolytic enzymes (protein-splitting ferments, proteases) produced by bacteria behave much like trypsin. Protein decomposition is known as *putrefaction*. Some authorities restrict the term "putrefaction" to the decomposition of proteins by anaerobic bacteria, which results in the formation of ill-smelling decomposition products, and use the term "decay" for the decomposition of proteins by aerobic bacteria. The latter does not result in the formation of ill-smelling decomposition products. There are a number of enzymes produced by bacteria that do not break proteins down into simpler compounds but coagulate them. These are known as lab enzymes.

The term fermentation has been used in two senses: in its narrow sense, to indicate the breaking down of carbohydrates by enzymes; in its broad sense, to indicate not only the break-

ing down of carbohydrates, but also the breaking down of proteins, fats, acids, and other substances by enzyme action. The present tendency is to use the word in its narrow sense. The process of fermentation is a complicated process and takes place in many ways. A simple illustration of fermentation, which is not as simple as the equation which shows only the end products indicates, is the breaking down of grape sugar into alcohol and carbon dioxide by yeasts. The change is indicated by the following equation:



This reaction forms the basis of both the manufacture of alcoholic beverages and baking. The products of fermentation depend on the kind of sugar, the type of enzyme present, and the condition under which the fermentation takes place. For instance, the yeast enzymes which break down glucose into carbon dioxide and alcohol are without effect on sucrose (cane sugar), while certain other enzymes acting on glucose change it to lactic acid instead of alcohol and carbon dioxide.

The fermentation reactions of bacteria are of importance in manufacturing and form one of the basic principles by which bacteria are classified. From their fermentative action on sugars bacteria are classified as (a) those that do not ferment certain sugars, (b) those that ferment certain sugars with the production of acid only, and (c) those that ferment certain sugars with the production of both acid and gas. The most common products of bacterial fermentation are lactic acid, formic acid, acetic acid, butyric acid, alcohol, and the gases—carbon dioxide and hydrogen. The fat-splitting enzymes produced by bacteria are not well understood.

Ptomaines.—When proteins are partially decomposed by bacteria in the absence of oxygen, certain crystalline, poisonous, basic substances known as *ptomaines* are formed. They are not products of the bacterial cell but arise from the material which the bacteria are decomposing. Their toxicity depends more on the nature of the material on which the bacteria are growing than on the bacteria them-

selves. Ptomaine poisoning was once thought to be very common, but it is now well known that the acute intestinal upsets following the eating of certain foods are due to bacteria or their toxins and not to ptomaines.

Nitrification, Nitrogen Fixation, and Denitrification.—
(See page 173.)

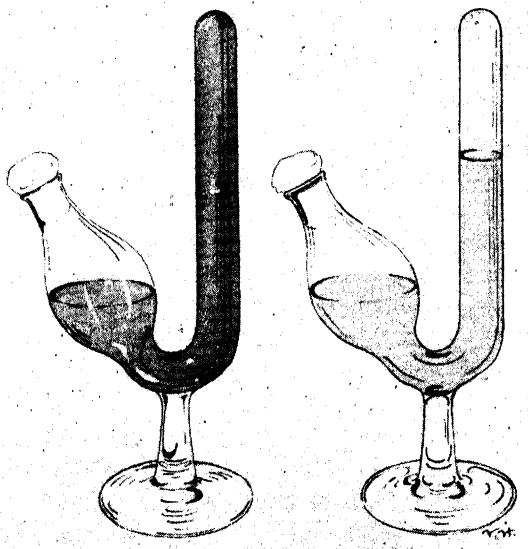


Fig. 28.—Smith fermentation tubes. Note that the closed arm of the tube on the left is filled with liquid, while that of the one on the right is partially empty. The liquid in the tubes is a solution of a fermentable sugar. The tube on the left is uninoculated or is inoculated with a species of bacteria which will not ferment the sugar. The tube on the right is inoculated with a species of bacteria which fermented the sugar with the formation of gas. The gas formed collected in the closed arm and displaced part of the liquid.

Toxins.—Practically all species of bacteria produce poisons known as toxins and in some the toxin is almost entirely responsible for the specific action of the bacteria. Toxins are of two types: *exotoxins* which are diffused by the bacterial cell into the surrounding medium and *endotoxins* which are liberated only when the bacterial cell is destroyed. Some bacterial exotoxins are more deadly than any mineral poison. Comparatively few bacteria produce exotoxins. The bacteria that are noted for their exo-

toxin production are: *C. diphtheriae*, *Cl. tetani*, *Cl. botulinum* and *Cl. welchii*. Less important from the standpoint of exotoxin production are certain strains of streptococci and *Bact. dysenteriae*. In diseases due to these organisms the bacteria grow locally and within themselves produce little effect, but the toxins that they elaborate at the site of growth are absorbed into the body to cause most serious

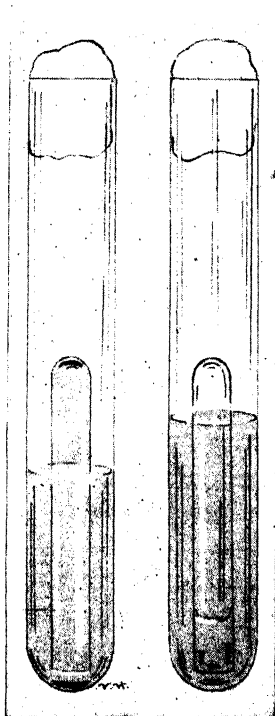


Fig. 29.—Dunham fermentation tubes. Note that the inverted tube on the left is filled with liquid while the one on the right is partially empty. See Fig. 28 for explanation.

and often fatal illnesses. When the exotoxin-producing organisms are grown in a liquid culture medium and are completely removed by filtration the toxins remain in the medium. When the toxin-containing medium is injected into a susceptible animal in the proper amount the disease is produced. If injected in a suitable amount into an ani-

mal suitable for antitoxin formation, antitoxin is produced in the body of the animal. Exotoxins are specific; i.e., diphtheria bacilli elaborate toxins that cause diphtheria and nothing else, while tetanus bacilli elaborate toxins that cause tetanus and nothing else, etc. When the exotoxin that causes a certain disease is treated with formaldehyde, it no longer causes the disease when injected into the body but produces an immunity to the disease. Such modified toxins are known as *anatoxins* or *toxoids*. Toxoids are used to produce a permanent immunity to diphtheria and tetanus.

Practically all bacteria contain endotoxins and this is the only kind possessed by most of them. As has been stated, endotoxins are liberated only when the bacterial cells disintegrate. They are not found in the surrounding medium when bacteria are grown in a liquid. They do not promote the formation of antitoxins and do not possess the specificity of exotoxins.

Hemolysins, Leucocidins, Coagulase, and Fibrinolysin.—*Hemolysins* are substances which cause the lysis (dissolving) of red blood cells. One hemolysin, but not the only kind, is that produced by bacteria. The presence of hemolysins may be demonstrated by growing the bacteria on agar containing whole blood. If hemolysins are present, the colonies will be surrounded by a clear colorless zone or a greenish zone. The hemolysins producing a clear colorless zone are known as *beta* hemolysins and those producing a green zone are known as *alpha* hemolysins. *Leucocidins* are substances that destroy polymorphonuclear leucocytes. These are the leucocytes that take an active part in the battle of the body against acute infections. *Coagulase* is a substance that causes the blood to clot more rapidly. *Fibrinolysin* is a substance that dissolves or destroys fibrin and, since a blood clot consists of blood cells enmeshed in interlacing strands of fibrin, causes the blood to clot slowly and liquefies clots already formed. The relation of hemolysins, leucocidins, and coagulase to immunity is not known. There seems to be a definite relation between fibrinolysin and immunity because fibrinolysin destroys blood clots which form around the site

of infection to wall it off. Hemolysins are formed chiefly by streptococci and staphylococci. Leucocidins are formed by pneumococci, streptococci, and staphylococci. Coagulase is formed by staphylococci and the detection of its formation is one of the methods of identifying these organisms. Fibrinolysin is formed by certain species of streptococci.

Spreading Factor.—This is a substance secreted by certain bacteria which causes the tissues to be more permeable to the bacteria elaborating the factor. The spreading factor is produced by pneumococci and streptococci.

Pigment Production.—So far as is known, pigment production has no relation to disease and has no importance other than serving as an aid in identifying pigment-producing organisms. Yellow pigments are most common, but pigments of almost any color may occur. The red and yellow pigments probably belong to the same chemical group as those of turnips, egg yolk, and fruits. Pigments are produced by both parasitic and saprophytic bacteria, but most species of bacteria do not produce pigments. Common pigment producers are *Staphylococcus aureus*, which produces a golden pigment, and *B. pyocyaneus*, which produces a bluish green pigment. *B. prodigiosus*, a nonpathogenic organism, produces a red pigment. Pigment-producing bacteria lose that property when grown under unfavorable conditions.

Heat Production.—During the growth of all bacteria heat is produced, but it is of such small amount that it can be detected in ordinary cultures only by most delicate methods. The heating of damp hay is in part due to bacterial action.

Light Production.—A few species of bacteria have the ability to produce light. Most of them live in salt water and some live a parasitic existence on the bodies of salt-water fish. Fox fire seen on decaying organic material, especially in the woods, is due to luminescent bacteria. None of the light-producing bacteria is pathogenic.

Odors.—Certain odors are characteristic of some species of bacteria, while others arise from the decomposition of the material in which the bacteria are growing.

True-False Test

Place the word "true" or "false" before each statement.

- 1. All cells probably produce some form of enzyme.
- 2. Complex food materials broken down by bacterial enzymes cannot be assimilated by the bacteria.
- 3. Bacterial enzymes are often more resistant to disinfectants than the bacteria that produced them.
- 4. The toxicity of ptomaines depends more on the nature of the material on which the bacteria are growing than on the bacteria themselves.
- 5. In some bacteria, toxins are almost entirely responsible for the specific action of the bacteria.
- 6. Exotoxins are liberated only when the bacterial cell is destroyed.
- 7. Exotoxins are never specific.

Completion Test

- 1. List the important bacterial activities which are responsible for the changes that the bacteria bring about.
- 2. ----- are substances produced by living cells that are capable of bringing about chemical change without undergoing any change themselves.
- 3. List four striking characteristics of enzymes.
 - a. -----
 - b. -----
 - c. -----
 - d. -----
- 4. Enzymes may be classified as ----- and -----.
- 5. Enzymes formed within the cell and extruded through the cell membrane into the surrounding medium are classified as -----.
- 6. Protein decomposition is known as -----.
- 7. What is the basic difference between putrefaction and fermentation?
- 8. ----- are formed when proteins are partially decomposed by bacteria in the absence of oxygen.
- 9. Toxins are of two types; namely, ----- and -----.
- 10. Three bacteria noted for their exotoxin production are -----, -----, and -----.
- 11. Discuss the characteristics of bacteria producing exotoxins relative to their ability to bring about an immunity.
- 12. Of what value are the pigments produced by bacteria to the bacteriologists?
- 13. To what is the phosphorescence of the sea partly due?

References

- Zinsser and Bayne-Jones: A Textbook of Bacteriology, New York, 1939, D. Appleton-Century Co.
- Jordan, Edwin O., and Burrows, William: Textbook of Bacteriology, Philadelphia, 1945, W. B. Saunders Co.
- Topley and Wilson: Principles of Bacteriology and Immunology, Baltimore, 1946, Williams & Wilkins Co.

CHAPTER VIII

METHODS OF STUDYING BACTERIA

EXAMINATION OF UNSTAINED BACTERIA- STAINING METHODS

The bacteriologist has a number of ways to study bacteria. He may take material directly from the site of disease and examine it in the unstained state or, as is more often the case, he may apply various staining methods. He may make a culture from the site of disease and after the bacteria have multiplied sufficiently, study them in the unstained state, apply stains, observe their cultural characteristics and use numerous other diagnostic procedures such as a determination of their biological activities. He may inject some of the bacteria taken from the site of disease or from a culture into a suitable animal and observe their effect on the animal. Lastly he may apply certain well-known immunological procedures.

The procedures used in the identification of bacteria may be classified as: (1) examination of unstained bacteria, (2) staining methods, (3) cultural methods, (4) animal inoculation, and (5) immunological methods. Immunological methods will be discussed in the chapter on immunity.

I. Examination of Unstained Bacteria

It is often desirable to examine unstained bacteria to determine their grouping, whether or not they are motile, and their reaction to chemicals or specific serums. These characteristics are usually determined by means of hanging-drop preparations. A few species of bacteria cannot be stained in accordance with the methods to be discussed in the next section or are so distorted by staining that their characteristic appearance is destroyed. Bacteria such as these are often examined by dark-field illumination.

Hanging-Drop Preparations.—To make a hanging-drop examination we must use, in addition to the microscope, (1) a

platinum loop for transferring the material to be examined, (2) a hanging-drop slide, and (3) a cover glass.

The platinum loop is a piece of fine platinum wire, about three inches in length, one end of which is fastened in a handle while the other end is fashioned into a loop about one-sixteenth of an inch in diameter. Platinum is used for making loops because this metal can be repeatedly sterilized by heating in a flame without being destroyed and quickly cools after being heated.

A hanging-drop slide is a piece of glass about the thickness of window glass and about one inch wide and three inches long with a circular concavity at its center. A cover glass is a piece of very thin glass about seven-eighths of an inch square.

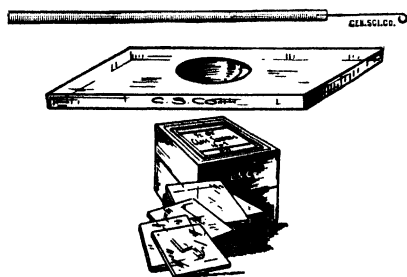


Fig. 30.—Platinum loop; concave slide; cover glasses. (Courtesy of Central Scientific Co.)

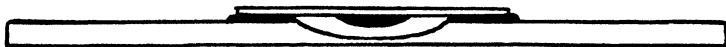


Fig. 31.—Diagrammatic illustration of a cross-section of a hanging-drop slide. Note the drop of material to be examined hanging from the bottom of the cover glass.

The preparation is made as follows: A little petroleum jelly is spread around the concavity of the slide. If the material to be examined is a culture growing on a solid medium or thick material taken from the site of disease, such as thick pus, a drop of salt solution is placed in the center of the cover glass and a loopful of the material is thoroughly mixed with it by means of the platinum loop. If bacteria growing in a liquid medium are to be examined, a drop of the medium is transferred to the cover glass by means of the

loop. The cover glass is inverted over the concavity in such a way that the drop to be examined hangs from the bottom of the cover glass but does not touch the surface of the concavity at any point. The preparation is now ready for examination. The petroleum jelly holds the cover glass in place and prevents evaporation.

In examining hanging-drop preparations Brownian motion and the flowing of organisms with currents in the preparation should not be mistaken for true motility. The platinum loop should be sterilized immediately before and after each transfer of bacteria-containing material. Since hanging-drop preparations contain living bacteria, the slide and cover glass should be sterilized after the examination is finished.



Fig. 32.—A dark-field preparation. Note the white organisms against the black background. 1, *Treponema pallidum*; 2, nonpathogenic spiral organisms. (From Bray: *Synopsis of Clinical Laboratory Methods*. The C. V. Mosby Co.)

Dark-Field Illumination.—As has been stated, dark-field illumination is used in examining bacteria that are too fine to be examined in the ordinary manner in the living state or cannot be stained by ordinary methods or are so distorted by staining that their identifying characteristics are lost. It finds its greatest usefulness in demonstrating *Treponema pallidum* in chancres and other syphilitic lesions. The material to be examined is placed on an ordinary slide and covered with a cover glass. We have found that sealing the cover glass to the slide with a ring of melted paraffin is very useful because it prevents slipping of the cover glass and accidental infection of the fingers.

Dark-field illumination depends on the use of a substage condenser so constructed that the light rays do not pass directly through the objects being examined but strike them at almost a right angle to the objective of the microscope. This gives the microscopic field a dark background against which bacteria or other particles appear as bright silvery objects. The dark-field microscope is of value in examining many organisms other than *Treponema pallidum*.

II. Fixing and Staining Methods

The bodies of bacteria are so small and delicate that when examined in hanging-drop preparations little of their finer structure can be made out, and in order to study them more closely, they must be colored with some dye. This process is called *staining*. The dyes most often used are aniline dyes

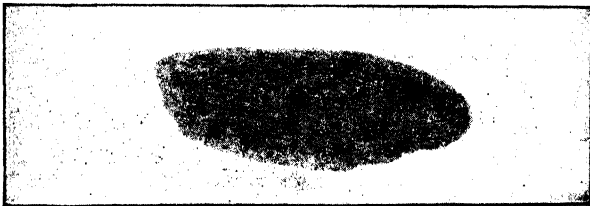


Fig. 33.—A properly prepared smear. (From Pieltt: *Pathology for Nurses*. F. A. Davis Co.)

and are derivatives of the coal tar product, aniline. To make a stained preparation a small amount of the material to be examined is placed on a perfectly clean slide and spread out into a thin film by means of a platinum loop or swab. The film is known as a *smear*. The smear is allowed to dry in the air and the slide, smear side up, is slowly passed through a flame two or three times. The flaming kills the bacteria in the smear and causes them to stick to the slide. This is known as *fixing*. Other methods of fixing are frequently used, but heat is most suitable for routine work. Among the other methods used are immersion in wood alcohol or Zenker's solution. When the smear has been fixed, the stain is applied and washed off with water, after which the slide is dried by blotting between sheets of absorbent paper.

There are four classes of stains used in bacteriology: (1) general stains, (2) differential stains, (3) stains for special bacteria, and (4) stains for certain parts of bacteria.

General Stains.—A general stain is usually an aqueous or alcoholic solution of a dye which is applied to the smear from one to five minutes and then washed off. Sometimes the solution has added to it a chemical that makes it stain more intensely. Such chemicals are called *mordants*.



Fig. 34.—Technician making smear. After the material is evenly spread on the slide, the smear is "fixed" by passing through a flame. In some cases the smear is fixed by treating with a chemical.

The most common general stains are Loeffler's alkaline methylene blue, carbolfuchsin, gentian violet, and safranin. To stain with any of these, the smear is fixed in the usual way and the stain is poured over it. The length of time the stain remains on the smear depends on the avidity with which it acts. After staining is complete, the stain is washed off with water and the slide is dried by blotting. The preparation is ready for microscopic examination. Most bacteria stain easily and quickly with general stains; some do

not stain so easily and a few do not stain at all. Capsules and spores are not stained with these stains but appear as clear unstained structures. Flagella do not stain at all and cannot be seen in the preparation.

Differential Stains.—Certain more complex staining methods divide bacteria into groups, depending on their reaction to the staining method used. Of these methods Gram's method and staining for acid-fast bacilli are most often used.



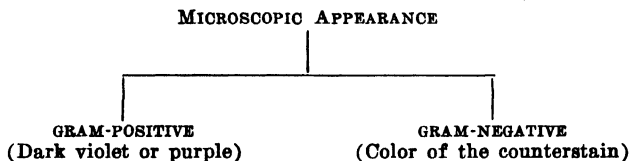
Fig. 35.—Technician staining smear. The slide on which the smear is made rests on a rack which is supported by a pan. The pan catches the stain when it is washed off the slide.

Gram's Method of Staining.—Gram's method of staining divides bacteria into two great groups: those that are gram-positive and those that are gram-negative. This method depends on the fact that when bacteria are stained

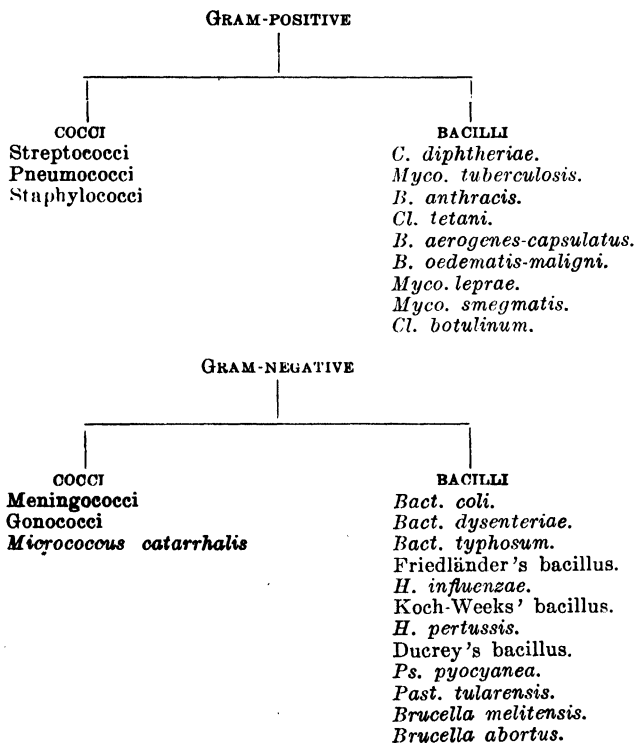
with certain dyes, such as methyl violet or gentian violet, and the smear is then treated with a weak solution of iodine, the bodies of certain species of bacteria form a combination with the dye and iodine to produce a color that cannot be removed by alcohol, acetone, aniline, etc., while in other species the color is readily removed by these solvents. Bacteria from which the color cannot be removed are spoken of as being gram-positive while those from which it can be removed are spoken of as being gram-negative. The reaction of bacteria to Gram's method of staining has no relation to their disease-producing powers, but it is of great aid in identifying them. Many technics have been devised for staining according to Gram's method. The method outlined below is often used. The explanations appended will apply to any technic used.

1. Make thin smear and fix in flame.
2. Stain with methyl violet or gentian violet—two minutes.
3. Wash stain off with water.
4. Cover smear with Gram's iodine solution—one minute.
5. Wash off iodine solution. (Both gram-positive and gram-negative bacteria are now stained a dark violet or purple color.)
6. Dip in alcohol or acetone until no more color flows from the smear. (All gram-negative bacteria are completely decolorized. The gram-positive ones are not affected.)
7. Cover smear with a stain that gives a contrast in color.
8. Wash with water, blot dry, and examine.

(Stains used for the purpose of giving a contrast in color are known as *counterstains*. The ones most often used in Gram's method are dilute carbolfuchsin and safranin, both of which give a red color, and Bismarck brown which, as its name implies, gives a brown color. Gram-negative bacteria are stained with the counterstain. Gram-positive bacteria do not stain with the counterstain because they are completely stained with the stain-iodine-bacterial cell combination that gives them their gram-positive characteristics.)



The following outline gives the reaction to Gram's stain of the most important pathogenic bacteria:



A few species of bacteria are gram-variable, but their number is so small that the value of the method is little affected.

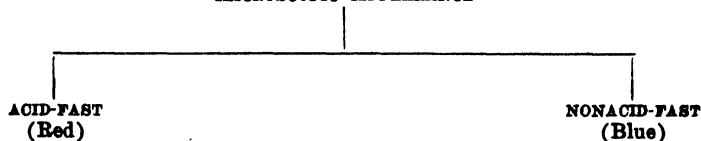
Staining for Acid-Fastness.—If bacteria are stained with certain dyes, of which carbolfuchsin is the best example, and the smear is then treated with an acid, it will be found that most species stain easily but are completely decolorized by the acid, while a few species stain with difficulty

but once stained retain the stain when treated with an acid. The species that retain the stain are spoken of as being acid-fast. The property of being acid-fast is most likely due to the presence of waxy substances in bacteria, especially in their cell membranes.

The technic of determining acid-fastness, outlined below, finds its practical application in the staining of sputum for *Myco. tuberculosis* because this bacillus is the only acid-fast organism commonly found in the sputum. The following is the technic and its explanation:

1. Make smear on slide and fix.
2. Flood slide with carbolfuchsin (red) and gently steam over flame (do not boil) for two or three minutes.
3. Wash off the excess of stain (all bacteria are now red).
4. Dip slide repeatedly in acid-alcohol, washing between times until all the red color is removed from smear. (At this step the acid has removed the red color from all bacteria that are not acid-fast. The acid-fast organisms are unaffected and remain stained a bright red color.)
5. Apply a stain that will give a contrast in color. (Loeffler's alkaline methylene blue is most frequently used. The acid-fast organisms are completely saturated with the red carbolfuchsin and, therefore, will not take up any of the blue counterstain. The nonacid-fast organisms, having had all their stain removed by the acid, stain deeply with the counterstain.)

MICROSCOPIC APPEARANCE



There are three important acid-fast organisms encountered in medicine: *Myco. tuberculosis*, *Myco. leprae*, and the nonpathogenic smegma bacillus which is of importance because it is a normal inhabitant of the genitalia and may be mistaken for *Myco. tuberculosis* in the urine. This may be avoided

by collecting the urine in such a manner as to exclude this organism. There are several species of nonpathogenic bacteria that are weakly acid-fast. Such organisms are often found in milk and butter.

Stains for Specific Organisms.—Important among the organisms that are stained by special means are *Treponema pallidum*, Negri bodies, etc.

Stains for Certain Parts of Bacteria.—Important methods of this type are stains for capsules, stains for spores, stains for flagella, and stains for metachromatic granules. Stains that have for their primary purpose the demonstration of metachromatic granules are especially valuable in identifying diphtheria bacilli and in differentiating them from related organisms. Important stains of this type are Albert's stain and Neisser's stain.

Questions for Review

1. How would you make a simple stain?
2. Name two very important differential stains. Give the underlying principles of each.
3. Name: (1) two important gram-positive cocci, (2) three important gram-positive bacilli, (3) two important gram-negative cocci, (4) three important gram-negative bacilli.
4. Name three important acid-fast bacilli. Why is each of importance?
5. Name: (1) some stains for special organisms, (2) same stains for special parts of organisms.

True-False Test

Place the word "true" or "false" before each statement.

- 1. In making a hanging-drop examination, the drop of the material is placed in the concavity of the hanging-drop slide.
- 2. In examining the hanging-drop preparations, Brownian motion and the flowing of organisms with currents in the preparation should not be mistaken for true motility.
- 3. The slide and cover glass should be sterilized after a hanging-drop examination has been made.
- 4. The main reason for sealing the cover glass with melted paraffin while making a dark-field study is to keep the medium from evaporating.
- 5. The finer structures of bacteria may be obtained by the hanging-drop method of examination.
- 6. By passing the smear through a flame two or three times, the bacteria are fixed to the slide.

- 7. In using general stains (usually an aqueous or alcoholic solution of a dye), the flagella may be seen clearly.
- 8. Spores and capsules appear as clear, unstained structures with such dyes as Loeffler's alkaline methylene blue, carbol-fuchsin, gentian violet, etc.

Completion Test

1. List five methods of studying bacteria.
 - a. -----
 - b. -----
 - c. -----
 - d. -----
 - e. -----
2. By means of the hanging-drop method in examining bacteria, such information as -----, -----, and ----- may be determined.
3. A ----- is used in making a hanging-drop examination to transfer the material to be examined to the slide.
4. Two reasons for using dark-field illumination in studying certain species of bacteria are:
 - a. -----
 - b. -----
5. The greatest usefulness of dark-field illumination has been found in demonstrating -----.
6. How is the dark background obtained in making a dark-field examination?
7. The process by which bacteria are studied by using a colored dye is known as a ----- method.
8. The dyes most often used are ----- dyes.
9. The spreading out of a small amount of the material to be examined on a clean slide into a thin film by means of a platinum loop is known as the process of making a -----.

References

- Kolmer and Boerner: Approved Laboratory Technic, New York, 1945, D. Appleton-Century Co.
- Gradwohl, R. B. H.: Clinical Laboratory Methods and Diagnosis, St. Louis, 1948, The C. V. Mosby Co.
- Zinsser and Bayne-Jones: Textbook of Bacteriology, New York, 1939, D. Appleton-Century Co.
- Stitt, Clough, and Branham: Practical Bacteriology, Haematology and Parasitology, Philadelphia, 1948, P. Blakiston's Son and Company.
- Topley and Wilson: Principles of Bacteriology and Immunology, Baltimore, 1946, Williams & Wilkins Co.
- Schaub, Isabelle G., and Foley, M. Kathleen: Diagnostic Bacteriology, St. Louis, 1947, The C. V. Mosby Co.

CHAPTER IX

THE STUDY OF BACTERIA BY CULTURAL METHODS AND ANIMAL INOCULATION

Their small size and the similarity in appearance and staining reactions of many species often make the identification of bacteria, by microscopic methods alone, impossible. One of the most important methods of identifying bacteria is by observing their growth on artificial food materials prepared in the laboratory. This is known as *culturing*. The food material on which bacteria are grown is known as a *culture medium* (pl. media), and the growth itself is known as a *culture*. A culture containing only one kind of bacteria is known as a *pure culture*; one containing two or more kinds is known as a *mixed culture*. Not only in identifying bacteria are cultural methods of value, but also in finding bacteria, for when infectious material is placed on a suitable culture medium, each bacterium present multiplies many times.

Culture Media.—For the most satisfactory growth of bacteria on artificial food materials, the proper temperature, moisture, and oxygen conditions must be provided, and the culture medium must contain the necessary nutritive principles and must be of the proper degree of alkalinity or acidity. The first three requirements are secured without any great difficulty, but the provision of a satisfactory culture medium is not so easy. Most disease-producing bacteria require complex foods similar in composition to the fluids of the animal body. For this reason the basis of many culture media is an infusion of meat prepared by soaking lean beef in twice its weight of water in the ice box. After the mixture has stood for twenty-four hours it is pressed through muslin. The meat is discarded and the liquid which is to be the basis of the medium is filtered through filter paper. In some cases a watery solution of commercial meat extract is substituted for the meat in-

fusion. Sterilization destroys the food value of some of the components of both meat infusion and solutions of meat extract. Peptone, a product derived from the partial breaking down of proteins, is often added in order to make up for the loss in nutritive value. To this basic medium which contains meat extractives, salts, and peptone, various other ingredients may be added.



Fig. 36.—Swab and culture media. From left to right; swab, slant of agar, tube of broth.

In many cases, in fact in most cases, it is desirable that the medium be a solid. In this case some ingredient that melts on heating and solidifies on cooling is dissolved in the liquid medium described above. The two best known solidifying agents used for this purpose are agar and gelatin. Agar is more often used. It melts completely at the temperature of boiling water and solidifies when cooled to about 40° C. The low temperature at which agar solidifies is very important because it is often desirable to inoculate infectious material directly into melted solid media which

could not be done if the agar began to solidify at a temperature high enough to kill bacteria.

Numerous enriching materials may be added to culture media. The most common ones are carbohydrates, blood serum, whole blood, bile, ascitic fluid, hydrocele fluid, etc. Carbohydrates are added for two purposes: (1) to increase the nutritive value of the medium and (2) to determine the fermentation reactions of the bacteria being studied. Blood serum, whole blood, ascitic fluid, etc., are added to promote the growth of the less hardy organisms. Dyes are often added to culture media. They serve two purposes: (1) they act as indicators to detect the formation of acid when the fermentation reactions of bacteria on carbohydrates are being studied or (2) they inhibit the growth of certain bacteria. An example of a dye used for the first purpose is phenol red which is red in an alkaline or neutral medium but becomes yellow if the medium becomes acid. An example of a dye used for inhibiting the growth of certain species of bacteria is gentian violet which inhibits the growth of most gram-positive bacteria.

The meat infusion or meat extract basis from which culture media are prepared is ordinarily highly acid. It is, therefore, usually necessary that the reaction of the medium be adjusted so that it is neutral or slightly alkaline because this is the reaction that is most suitable for the growth of most bacteria. A few species, however, grow on media that are slightly acid.

The reaction is adjusted by determining the acidity or alkalinity of the medium by titration or by colorimetric methods; if it is found to be too acid sufficient alkali to give the required reaction is added, and if it is found to be too alkaline sufficient acid to give the required reaction is added. Culture media are usually poured into test tubes or flasks. The containers are then closed with cotton plugs and sterilized. After sterilization tubes of solid media are usually laid on a flat surface with their mouths raised so that when the medium solidifies it is in a slanting position. This gives more surface for the bacteria to grow upon.

Cotton plugs allow the access of moisture and oxygen but prohibit the entrance of bacteria; therefore the medium remains sterile until used and bacteria with which it is inoculated are not contaminated by bacteria from the outside. Most media are sterilized by autoclaving. Those that contain carbohydrates have to be sterilized by the fractional method because many carbohydrates will not withstand the high temperature of the autoclave. Enrichment materials, such as blood serum and whole blood, that are injured by even moderate heat are collected in such a manner that they are kept sterile and mixed with the medium after it has been sterilized and allowed to cool. In the case of agar media these substances are added when the medium reaches 40°-42° C., because when the temperature falls slightly lower than this the agar begins to solidify.

Not all media are made according to the methods indicated above. For instance, Loeffler's blood serum medium which is used throughout the world for cultivating diphtheriae bacilli is made by mixing three parts of blood serum with one part of dextrose broth, placing in tubes slanting, and heating the tubes until the medium solidifies by coagulation of the serum.

While most every species of bacteria has some medium upon which it grows best and a few will grow only on media specially prepared for them, most of the pathogenic bacteria will grow more or less luxuriantly on the routine or standard media described above. In all, more than two thousand varieties of culture media have been described. Table I shows some of the media most suitable for the isolation and growth of the common pathogenic bacteria.

Selective and Differential Media.—Media which promote the growth of one organism and retard the growth of other organisms are known as *selective* media. Media which serve to differentiate organisms growing together are known as *differential* media. Examples of selective media are bismuth-sulphite agar and Petragnani's medium. Bismuth-sulphite agar is used in cultivating typhoid bacilli from feces. It promotes the growth of typhoid bacilli and retards the growth

of bacteria normally occurring in the feces. Petragnani's medium promotes the growth of tubercle bacilli and retards the growth of the other organisms. Examples of differential media are saccharose-mannitol agar and Russell's double sugar agar, both of which are used in the differentiation of the gram-negative bacteria occurring in the intestinal canal.

Sulfonamide and Penicillin Inhibiting Media.—When cultures are made on persons who have been taking certain of the sulfonamide drugs or penicillin, it may be necessary to incorporate in the culture medium some substance which will counteract the ability of these drugs to prevent bacterial

TABLE I

ORGANISM	MEDIA MOST SUITABLE FOR GROWTH
<i>Staphylococcus</i>	Grows on almost any medium.
<i>Streptococcus</i>	Blood agar; dextrose brain broth; tryptose phosphate broth (with 0.1 per cent agar).
<i>Pneumococcus</i>	Blood agar; tryptose blood agar; brain heart infusion broth.
<i>Gonococcus</i>	Proteose hemoglobin agar. Grows with difficulty on any medium.
<i>Meningococcus</i>	Tryptose blood agar; brain heart infusion broth. Grows poorly on most media.
<i>Micrococcus catarrhalis</i>	Grows abundantly on almost all media.
<i>Myc. tuberculosis</i>	Grows only on special media; growth very slow.
<i>C. diphtheriae</i>	Loeffler's blood serum.
<i>Bact. typhosum</i>	Nutrient broth; nutrient agar; bismuth sulphite agar; MacConkey's agar.
<i>Bact. dysenteriae</i>	Nutrient broth; nutrient agar; special media.
<i>Bact. paratyphosus</i> A and B	Same as <i>B. dysenteriae</i> .
<i>Bact. coli</i>	Same as <i>B. dysenteriae</i> .
<i>Brucella melitensis</i> and <i>Brucella abortus</i>	Tryptose agar.
<i>B. anthracis</i>	Grows on almost all media.
<i>Cl. tetani</i>	Dextrose broth with 0.2 per cent agar (anaerobic).
Gas bacilli	Deep cultures in dextrose agar (anaerobic).
<i>H. influenzae</i>	Blood agar; special media.
<i>Past. tularensis</i>	Blood cystein agar.
<i>Treponema pallidum</i>	Grows with difficulty on special media.

multiplication. If this is not done, enough of the drug to prevent bacterial multiplication may be introduced into the medium with the material being cultured, and, although bacteria are present, no growth will occur. If the patient has been taking the sulfonamide drugs, para-aminobenzoic acid, which counteracts the action of the sulfonamide drugs, is incorporated in the medium. If the patient has been taking penicillin, penicillinase (a substance produced by certain penicillin-resistant bacteria and which is capable of counteracting the ability of penicillin to prevent the multiplication of bacteria) is incorporated in the medium.

Making Cultures.—A culture is made by removing some of the material to be cultured, such as sputum, urine, or pus, with a platinum loop and dipping it into a fluid medium or rubbing it gently over the surface of a solid medium.

Cultures serve two purposes: (1) Each bacterium multiplies rapidly, and within a few hours there are many more in the culture than there were in an equal amount of the material from which the culture was made. Consequently bacteria are often easily found in cultures when they are found with difficulty or not at all by making smears of the material from which the culture was made. For instance, diphtheria bacilli can be found by throat cultures twice as often as by throat smears. (2) When a culture is made on a solid medium all of the bacteria that grow from each bacterium deposited on the medium cling together and form a mass of bacteria visible to the naked eye. These are called *colonies* and ordinarily make their appearance within eighteen to twenty-four hours. Colony characteristics, such as texture, size, shape, color, and adherence to the medium, are fairly constant for each species and are valuable in differentiating one species from another. Theoretically each organism gives rise to a colony but two or more organisms may cling together and when planted upon a medium give rise to only one colony. If organisms that cling together are of different kinds, the colony will contain different kinds of bacteria. As a rule, however, a colony contains only one kind of bacteria.

Often in place of making the culture on a slant of solid medium, the medium is melted and poured into a Petri dish. A Petri dish is a circular glass dish about three inches in diameter with perpendicular sides about one-half inch high. A cover exactly like it but with a little greater diameter is inverted over it. The tops of the sides are perfectly ground, and a container is thus formed which prevents either the entrance or exit of bacteria. Cultures made in these dishes permit a better study of colonies than those made on slants. Petri dish cultures are usually spoken of as "plates" and the process of making them as "plating."

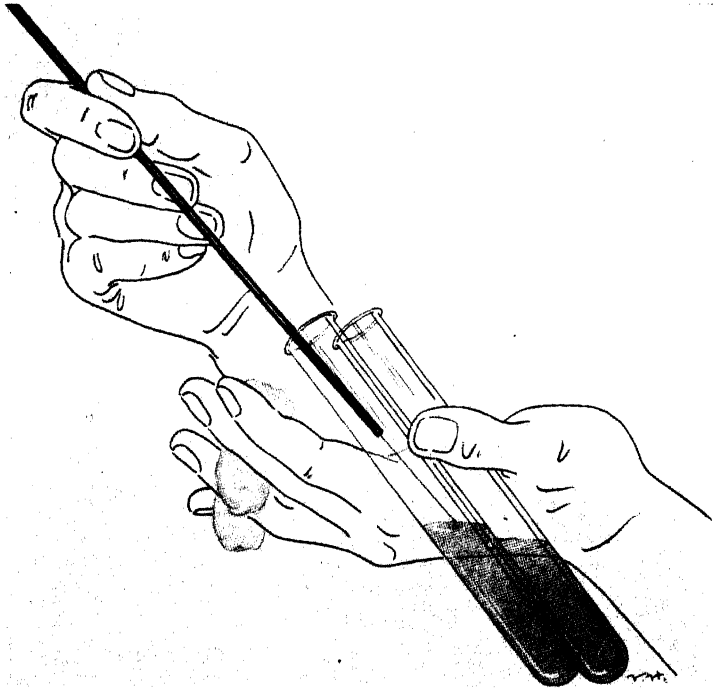


Fig. 37.—Inoculating a tube of liquid culture medium.

Pure Cultures.—As a rule, infectious material contains more than one kind of bacteria. To study one kind alone it must be separated from all other kinds and grown alone. The process is called obtaining a *pure culture*. Pure cul-

tures are usually obtained by the "pour plate" or "streak plate" method. The pour plate method is as follows:

1. Three tubes of agar are melted by placing in boiling water and then allowed to cool to 40° or 42° C. At this temperature the medium is liquid but not hot enough to injure bacteria. If an enriching material, such as blood serum or whole blood that is injured by heat, is to be added to the medium, it is added at this time.
2. A loopful of the material from which we expect to obtain a pure culture is transferred to one of the tubes. The plug is replaced in the tube and the tube is rolled between the palms of the hands to completely distribute the bacteria through the medium.
3. After the loop has been thoroughly sterilized, three loopfuls of the contents of the inoculated tube are transferred to the second tube. This further dilutes the bacteria.

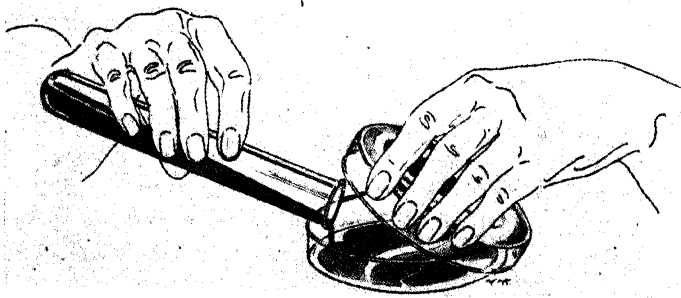


Fig. 38.—Pouring culture medium into Petri dish. Culture medium will not keep well in Petri dishes; therefore it is usually kept in tubes. Just before use it is melted and poured into the dishes. When it cools, it is ready to inoculate.

4. After the contents of the second tube have been mixed and the platinum loop has been sterilized, five loopfuls of the mixture are transferred to the third tube and mixed. This gives a still higher dilution of the bacteria.
5. The contents of each tube of medium are then poured into a Petri dish and allowed to solidify.
6. The dishes are incubated for twenty-four to forty-eight hours. Since each tube of medium contains fewer bacteria than the one preceding it, a dilution will finally be reached in which the bacteria are so few in number that when they grow into colonies in the Petri dish the colonies will be distinctly separated from each other. The colonies are carefully observed and those that are to be studied further are removed from the Petri dish with a straight platinum wire and rubbed over the surface of one or more slants

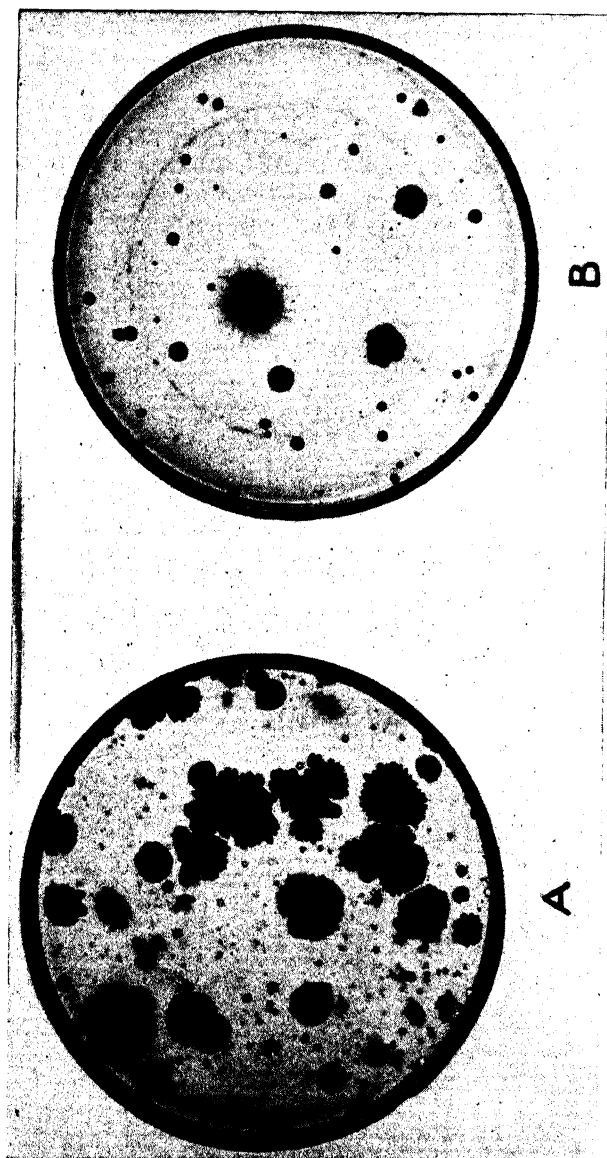


Fig. 39.—Petri dishes showing colonies of bacteria. Note the different sizes and shapes of colonies. This means that more than one species of bacteria are present. Plates A and B were obtained from different sources.

of suitable media. This is known as "fishing." If the colonies are not separated from each other, it is impossible to fish one colony without touching other colonies. After a colony has been studied on a plate (as Petri dish cultures are called) and transferred to slants, the slants are allowed to incubate for twenty-four to forty-eight hours, and these cultures are studied further. In the majority of cases all bacteria growing on a slant will be alike because they all grew from the members of a single colony on the plate, and these in turn grew from a single bacterium in the original material. If, as may sometimes happen, the colony contains two or more kinds of bacteria, the same two or

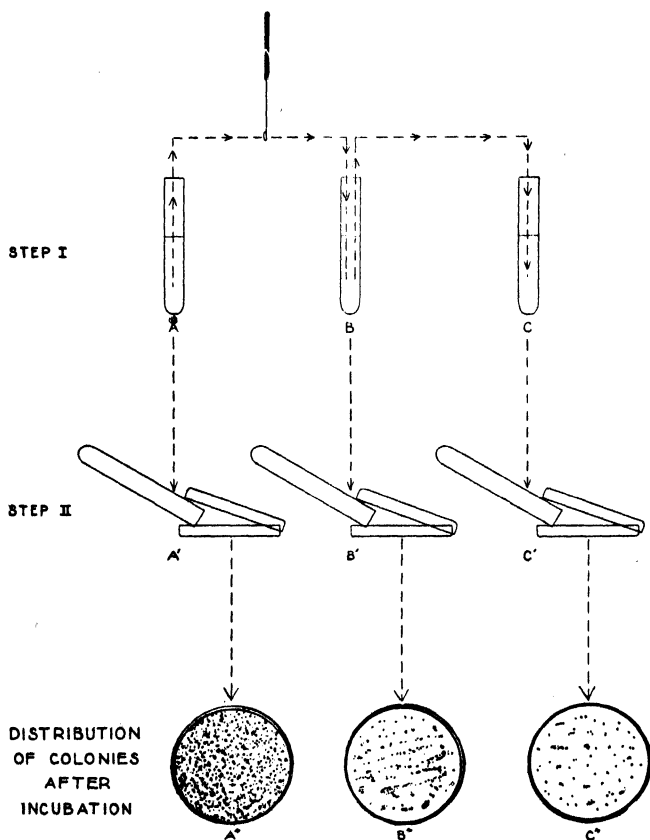


Fig. 40.—How a pure culture is obtained (diagrammatic illustration.) In step I tubes A, B, and C, which contain melted and cooled agar, are inoculated as indicated by the broken lines and arrows. Step II shows the transfer of each tube of the inoculated agar to a Petri dish. A'', B'', and C'' are actual photographs showing the distribution of colonies on the different plates. Note that it would be very difficult to "fish" a colony from A'', while it could be done with ease from C''.

more kinds of bacteria grow on the slant. In this case they are separated by suspending some of the bacteria from the slant in sterile salt solution and replating.

Streak Plates.—In some cases the medium is poured into Petri dishes and allowed to solidify after which a single loopful of infectious material is streaked over the surface of a first, second, and third plate without obtaining any fresh material with the loop. In this way so few bacteria are finally deposited on the surface of one or more plates that the colonies which develop from them are distinctly separated.

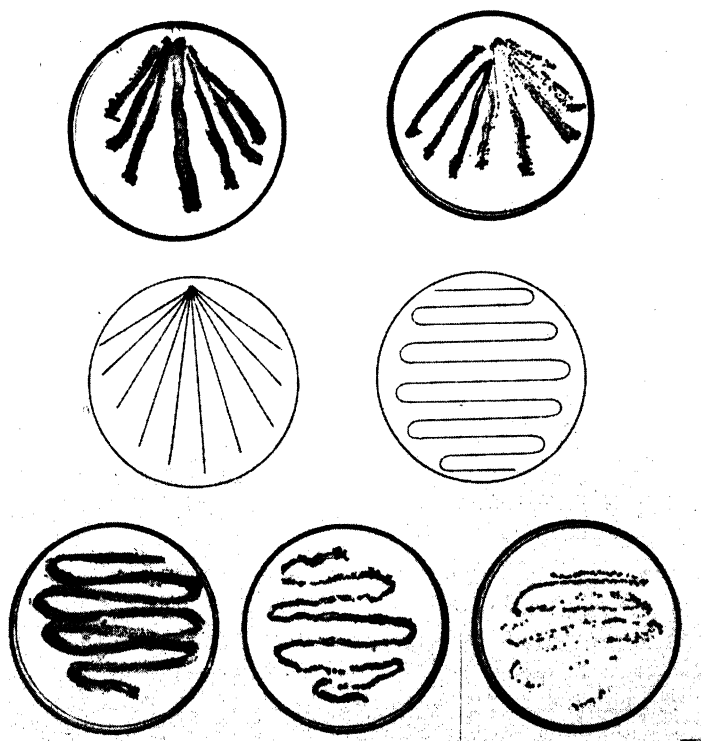


Fig. 41.—Obtaining a pure culture by the streak plate method. The drawings in the middle indicate the methods of streaking the plates with the loop containing the material from which a pure culture is to be obtained. The plates at the top were streaked according to the drawing on the left. Those at the bottom were streaked according to the drawing on the right. After one plate is streaked the next one is streaked without obtaining any new material with the loop. Note discrete colonies on plates to the right at both top and bottom.

How Pure Cultures Are Studied.—After a pure culture has been obtained, the bacteria may be studied from the following standpoints: (1) size, (2) shape, (3) motility, (4) staining reactions, (5) presence or absence of spores, capsules, and flagella, (6) cultural characteristics, and (7) pathogenicity (power to produce disease). Important cultural characteristics are: (1) optimum temperature, (2) aerobic or anaerobic growth requirements, (3) media most suitable for growth, (4) appearance of growth on different media, (5) action of bacteria on different media (example—some bacteria liquefy gelatin; others coagulate milk), (6) pigment production, (7) fermentation of carbohydrates, and (8) toxin production.

Determination of Fermentation Reactions of Bacteria on Carbohydrates.—This is a cultural characteristic of great constancy that is of extreme value in differentiating species. To determine the fermentation reactions of bacteria, media containing different sugars are inoculated with the bacteria and observed for gas production and acid formation. Gas production in liquid media is detected by the use of special tubes containing closed arms in which the medium is displaced by any gas that is formed. Solid media are inoculated for fermentation studies by taking up some of the bacteria with a straight needle and plunging the needle deeply into the solid medium. In some cases the medium is melted by heating, cooled to 40° C., and then inoculated. Gas production in solid media is indicated by disruption of the medium by gas bubbles. Acid formation in both liquid and solid media is indicated by color changes in indicators (see page 109) incorporated in the medium. The carbohydrates most often used in fermentation studies are dextrose, lactose, and saccharose, but many others may be used.

Counting Bacteria by Plating.—This method depends on the theory that when material containing bacteria is cultured, every bacterium develops into a colony. This is not strictly true because some bacteria may fail to multiply and, as has already been shown, two or more bacteria may cling together and form a single colony. Although the

method has these disadvantages it is of decided value in the examination of water and milk. The count is carried out as follows: four tubes containing 9 c.c. of sterile distilled water are provided. To the first tube 1 c.c. of the material to be examined is added and mixed. From this tube 1 c.c. is transferred to the second tube and mixed. From the second tube 1 c.c. is transferred to the third tube and mixed, and from the third tube 1 c.c. is transferred to the fourth tube and mixed. This gives a 1:10, 1:100, 1:1,000 and 1:10,000 dilution of the original material. With a sterile pipette transfer exactly 1 c.c. from each tube to a Petri dish and to each dish add sufficient melted agar.



Fig. 42.—Plating milk to determine how many bacteria it contains. The method here illustrated differs somewhat from that given in the text because previous examinations of this milk have shown that material and time will be saved by using duplicate 1-100 dilutions and averaging the two. From left to right are seen sterile wrapped Petri dishes, bottle of milk, two dilution bottles each containing 99 c.c. of water, flask of liquid medium, Petri dishes and wrapped sterile pipettes. The technician is placing 1 c.c. of diluted milk in a Petri dish. After this the liquid culture medium will be added. The water bath used to keep the culture medium at the proper temperature and the flame for sterilizing the mouths of the dilution bottles are not shown.

The agar should be cooled to 42° C. before adding. Mix contents of each dish by rotating and let solidify. Incubate for twenty-four to forty-eight hours and count the colonies that have developed. Let us say for instance that the sec-

ond plate shows 200 colonies. This means that at least 200 bacteria were present in the 1 c.c. of material placed in the tube and since this was a 1:100 dilution of the original material the latter must have contained at least 20,000 bacteria per cubic centimeter. More than this number of bacteria may have been introduced into the dish because some may have failed to grow and some may have clung together in groups of two or more that developed into single colonies. In other words the number of bacteria indicated by the count are certainly present and more may be present.

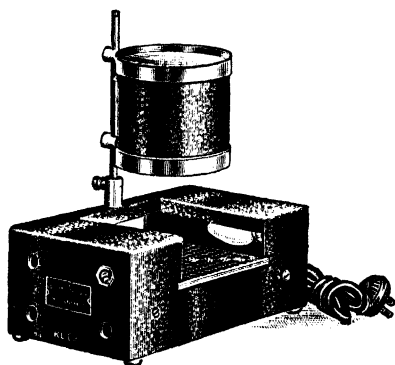


Fig. 43.—Apparatus for counting colonies. The Petri dish is placed on the central ruled table and the colonies are viewed through the magnifying lens above. The use of a low degree of magnification reduces eye-strain and makes very small colonies easily seen. (Courtesy of Greene Bros., Dallas, Texas.)

Culturing Anaerobic Bacteria.—Two methods are in general use. In the first method a culture tube about eight inches in length and about half full of medium is used. The tube is heated in a boiling water bath for several minutes to expel any oxygen that may be in the medium. The tube is quickly cooled and the material to be cultured is inoculated into the medium after which the culture is sealed by pouring a layer of sterile melted petroleum jelly about three-fourths of an inch thick upon the top of the medium. If an agar medium is used, the inoculation is made when the heated medium cools to a temperature of 42° C.

In the second method cultures are made in the ordinary manner and placed in a glass chamber so constructed that

the oxygen is removed by some chemical reaction that is made to take place in the chamber, or by replacing it with some gas, such as hydrogen, that does not have any effect on the growth of the bacteria.

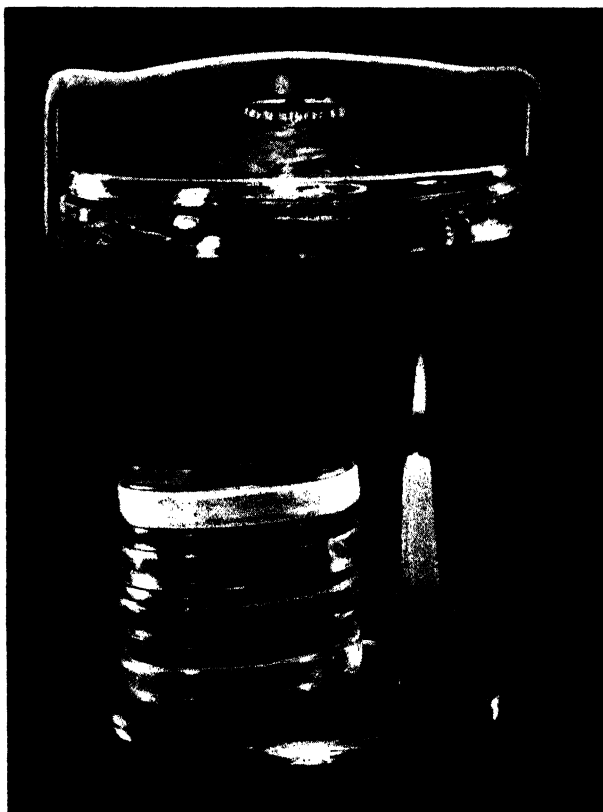


Fig. 44.—A simple method of obtaining an anaerobic condition for growing cultures. The cultures and a lighted candle are placed in a container and the container is made airtight. The candle burns until the oxygen is exhausted and then goes out.

Animal Inoculation.—The inoculation of suitable animals is of great value in the study of certain bacteria. After an animal has been inoculated, it is kept under observation to see what effects the bacteria will have. In some cases the animal is killed after a certain length of time and examined for evidence of disease. Smears and cultures may be made and

gross and microscopic changes in the organs observed. In other cases the animal is not killed, but blood and body fluids are removed at intervals for examination.

The animals most often used for inoculation are guinea pigs, white mice, white rats, and rabbits. The inoculations are given with an ordinary hypodermic syringe and are most often given subcutaneously (beneath the skin), intravenously (in a vein), intraperitoneally (into the peritoneal cavity), or subdurally (beneath the dura).

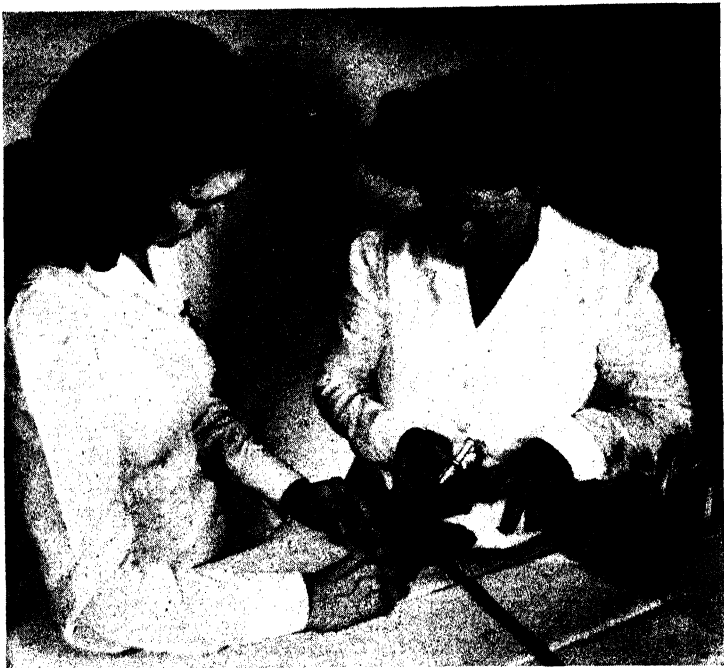


Fig. 45.—Inoculation of a guinea pig. The point of a needle is directed toward the lymph nodes in the inguinal region of the pig.

There are several reasons for performing animal inoculations:

1. In some cases bacteria are most easily detected by animal inoculation (ex. *Past. tularensis* and, under some conditions, *Myco. tuberculosis*).
2. It is used to determine the virulence of bacteria (ex. *Corynebacterium diphtheriae*).

3. It is sometimes the easiest way of obtaining bacteria in a pure culture.

4. It is often necessary in order to determine the action of drugs on bacteria.

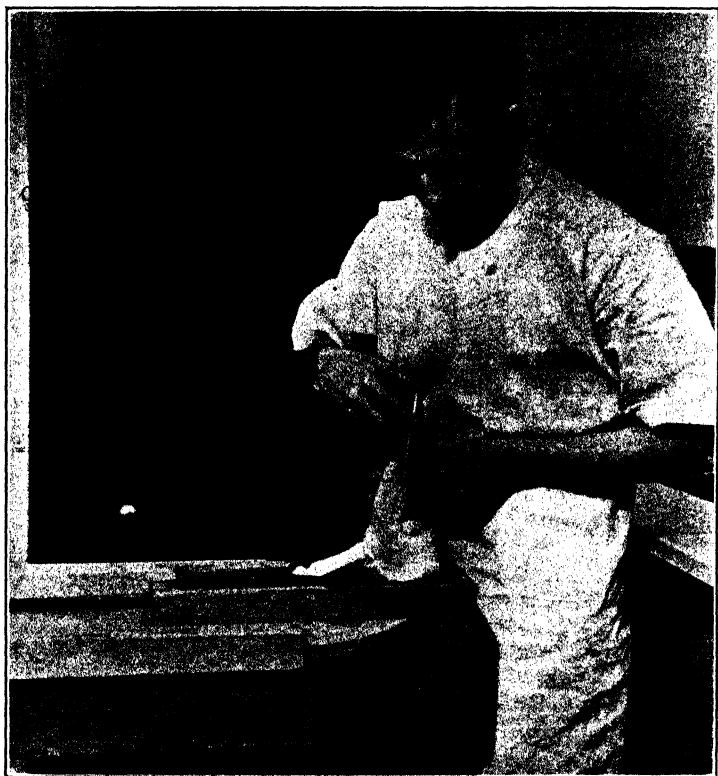


Fig. 46.—Inoculating a rabbit via the marginal vein of the ear. The rabbit is removed from the box by releasing the sliding lid.

A good example of animal inoculation being the best method of detecting the presence of bacteria is the ease with which tuberculosis of the kidney is often proved by injecting some urine into a guinea pig when the bacteria cannot be found by direct microscopic examination of the urine. A good example of animal inoculation being used to obtain a pure culture is seen in pneumococcus typing. Some of the sputum in which the type of pneumococcus is to be deter-

mined is injected into the peritoneal cavity of a white mouse and within a few hours the growth of pneumococci has outstripped that of all other organisms to such an extent that the peritoneal contents consist of an almost pure culture of pneumococci ready to be typed.

Questions for Review

1. What are the most common constituents of culture media?
2. Why is agar most commonly used as a solidifying agent in culture media?
3. What are the purposes of dyes in culture media?
4. What are the advantages of the culture over a smear in identifying bacteria?
5. Of what value is a study of colony formation in identifying bacteria?
6. What are the advantages of making cultures in Petri dishes?
7. Outline the steps in making a "pure" culture.
8. Of what value is the determination of the fermentation reaction of bacteria?
9. What are differential media? Selective media?
10. Briefly describe how bacteria are counted by culturing. What are some of the disadvantages of this method of counting?
11. What animals are most commonly used for animal inoculation, Explain the principles of animal inoculation.

True-False Test

Place the word "true" or "false" before each statement.

- 1. All bacteria can be identified by microscopic methods alone.
- 2. The bacterial count of water and milk is usually done by a process known as "plating."
- 3. For growing most bacteria the culture medium should be slightly acid.
- 4. The smear is more valuable in identifying bacteria than the culture.
- 5. Bacteria may be identified, in some cases, by the type of colony they form.
- 6. The determination of the fermentation reactions of bacteria on carbohydrates is of great value in differentiating species of bacteria.
- 7. In culturing aerobic bacteria, oxygen must be excluded from the plate or test tube.
- 8. The Petri dish is used when colonies of bacteria are to be studied.
- 9. Petri dish cultures are usually spoken of as "plates."

Completion Test

1. The food material on which bacteria are grown is known as a _____, and the growth itself is known as a _____.
2. A culture containing only one kind of bacteria is known as a _____ culture; one containing two or more kinds is known as a _____ culture.
3. For the most satisfactory growth of bacteria on artificial food materials, the following requirements must be met:
 - a. _____
 - b. _____
 - c. _____
 - d. _____
 - e. _____
4. Culture media are usually sterilized by _____.
5. After sterilization, culture media tubes should be laid on a flat surface with their mouths raised because _____.
6. Examples of organisms which require special media for growth are _____, _____, and _____.
7. After a "pure" culture has been obtained, the bacteria may be studied from the following standpoints:

a. _____	e. _____
b. _____	f. _____
c. _____	g. _____
d. _____	
8. Some of the cultural characteristics of bacteria which aid in the identification are:

a. _____	e. _____
b. _____	f. _____
c. _____	g. _____
d. _____	h. _____
9. The chief reasons for performing animal inoculations are:
 - a. _____
 - b. _____
 - c. _____
 - d. _____

References

(See References Chapter VIII.)

CHAPTER X

COLLECTION OF SPECIMENS FOR BACTERIOLOGICAL EXAMINATION

Let the person who collects specimens for bacteriological examination ever keep in mind two important facts: First, in the practice of scientific medicine bacteriological investigations often give the final diagnosis and determine the mode of treatment in the living and reveal the cause of death in the dead. Second, *the collection of the material to be examined is just as important as any other part of a bacteriological investigation* because, regardless of how well the remainder of the investigation is done, improper collection of the material to be examined will lead to erroneous results.

There are several rules that are applicable to the collection of any specimen for bacteriological examination: (1) the specimen should be collected in such a manner that it does not become contaminated with other bacteria (example—in making smears and cultures from the throat care should be taken not to contaminate the swabs with the secretions of the mouth), (2) sterile paraphernalia should always be used in collecting the specimen and the specimen should be put in a sterile container, (3) material used in collecting the specimen should be sterilized as soon as possible, (4) the specimen should be collected in such a manner that it does not become a source of danger to others (example—sputum or other excreta should not be allowed to get on the outside of the container), (5) whenever possible, smears should be made from the original material, (6) no preservative or antiseptic should be added to the specimen, (7) the specimen should be plainly labeled, stating the patient's name, source of specimen, and the organism or organisms suspected, (8) the specimen should be delivered to the laboratory immediately in order that the examination

may be begun as soon as possible, and (9) if the patient upon whom the culture is being made is receiving sulfonamide drugs or penicillin, a statement to that effect should accompany the specimen. This allows the laboratory to select media containing ingredients which counteract the inhibiting effects on bacterial growth of penicillin or any sulfonamide compound which may be in the specimen.



Fig. 47.—Special medium for blood cultures. The tube is inoculated by perforating the rubber stopper of the tube of medium with the needle of the syringe containing the blood and expelling the blood into the medium.

In making cultures the medium most likely to grow the suspected organism or organisms and, in addition, the medium most likely to grow any organism that might be present should be chosen. Blood agar is the medium that will come nearer growing any organism that may be present. Blood agar plates are superior to the tubed medium except in those cases in which the cultures are taken at a distance from the laboratory because plates are not easily transported.

Urine for bacteriological examination should be collected with a sterile catheter. Sometimes this may be dispensed with in the male by cleansing the meatus with soap and water and then scrubbing with 70 per cent alcohol. Catheterization should always be done in the female, and it should be seen that the parts are thoroughly cleansed before the catheter is introduced. In both voided and catheterized specimens the first portion should be discarded, and the last portion should be collected in a sterile container for examination.



Fig. 48.—Removing blood from vein at the bend of the elbow. Blood for culture, serological investigation and chemical analysis is secured in this manner. Strict asepsis must be observed.

Blood for cultures must be collected with special care because bacteria, especially staphylococci, are often present upon the surface of the skin and within its superficial layers. Blood cultures are made as follows: (1) paint the skin over the veins at the bend of the elbow with tincture of iodine, (2) remove the iodine with alcohol, (3) place an alcohol compress on the area and let it remain for one hour at which time the area is repainted with tincture of iodine

and the iodine is removed with alcohol. A tourniquet is secured, not too tightly, around the arm just above the elbow, and the patient is told to close and open his hand three or four times. A prominent vein is selected and punctured with a 20 c.c. syringe and from 10 to 15 c.c. of blood are removed. The blood is added directly to the culture



Fig. 49.—Technician inoculating tube of blood culture medium.

media or placed in a sterile bottle, containing sodium citrate to prevent coagulation, and carried to the laboratory where it is distributed to suitable culture media. The needle should be removed from the syringe before the blood is expelled because this prevents contamination. In young children blood may be secured from the external jugular vein and in those under one year of age it may be secured from the superior longitudinal sinus.

Blood for serological examinations such as the Wassermann test and the precipitin tests for syphilis and various agglutination tests for the continued fevers is collected from a vein at the bend of the elbow. The technic is the same as for collecting blood for a blood culture with the following exceptions: (a) the preliminary sterilization consists only of painting the area with tincture of iodine and removing the iodine with alcohol and, (2) the blood is placed in a chemically clean test tube and allowed to clot. Five cubic centimeters are sufficient.

Blood for the estimation of the sulfonamide compounds is collected in the same manner as that for serological examination with the exception that the blood is placed in a bottle containing an anticoagulant. Five cubic centimeters are sufficient. This is often done because sulfonamide therapy should be controlled by frequent estimations of the amount of the drug in the blood.

Blood for the estimation of penicillin is usually collected at hourly or half-hourly intervals over a period of four hours after the drug has been given. As a rule the blood is allowed to clot and the determination is made on the serum. In some cases an anticoagulant is added and the determination is made on the plasma. The serum or plasma should be placed in the ice box as soon as removed from the body and kept there until the determination is made.

Sputum is much more often improperly than properly collected. Many specimens consist of secretions from the nose and throat and contain no sputum at all. The sputum should represent a true pulmonary secretion and should be expelled after deep coughing. The teeth should be thoroughly scrubbed with paste, and the mouth rinsed with sterile water before the specimen is taken or else the sputum will be heavily contaminated with mouth bacteria. More sputum is often raised in the morning, and this sputum often contains *Myco. tuberculosis* when specimens taken later in the day do not. Bronchial secretions are sometimes secured by means of the bronchoscope. In infants a specimen may be obtained by swabbing the pharynx during coughing. When it is impossible to obtain a satisfactory specimen

of sputum the stomach contents may be examined for the presence of tubercle bacilli. The presence of tubercle bacilli in the stomach contents is due to swallowed sputum. This method of examination is of value in children. The ideal container for sputum is a two-ounce wide-mouthed bottle with a rubber stopper.

Cultures from the nose and throat are most often made in cases of suspected diphtheria but may be made in many other conditions. The purpose of the examination is often defeated by taking the culture just after an antiseptic has been used because the antiseptic retards the growth of any bacteria that may be present. This applies to other cultures as well as throat cultures. In making throat cultures a good light must be used and so far as is possible the swab should be allowed to come in contact with only the diseased area. In taking cultures from the nose a small tightly wound swab is passed directly back through the nose. Large loose swabs are to be avoided because they may come off of the applicator and remain in the nose. Many more cases of diphtheria will be detected when cultures are made from both nose and throat than from the throat alone. In no case should any great reliance be placed in a failure to find *C. diphtheriae* in smears made directly from the nose and throat because the organisms are often found in abundance in cultures after they have not been found in direct smears. Although this is the case, smears should always be made when diphtheria-like lesions of the throat are encountered because the lesions of Vincent's angina, the causative organisms of which are detected only in smears, often bear a marked resemblance to the membrane of diphtheria.

In making examinations to detect meningococcus carriers the cultures are not made from the throat but from the nasopharynx which is the upper portion of the throat back of the soft palate. In place of using an ordinary swab the cotton is wrapped around the end of a piece of wire bent at right angles about one inch from the end. In taking specimens from the throat and nasopharynx care should be taken to avoid contaminating the swabs with saliva.

Feces for ordinary bacteriological examination may be collected in sterile sputum bottles. The examination for typhoid bacilli is facilitated by collecting the feces in a special brilliant green bile medium because bile facilitates the growth of typhoid bacilli and brilliant green retards the growth of many other intestinal organisms. If amebas are suspected, the specimen should be kept warm until it reaches the laboratory, because amebas soon lose their motility if allowed to become cold. The specimen is passed into a vessel which has been warmed. A portion is then placed in a small bottle, which is tightly corked. This small bottle is placed in a fruit jar which has been filled with water just a few degrees above body temperature. This will keep the specimen warm for a considerable time. In hospital practice the specimen may be sent to the laboratory at once, without this special preparation.

Pus from abscesses and boils may be obtained by painting the abscess or boil with tincture of iodine, allowing it to dry, and incising with a sterile scalpel. Some of the contents are obtained by means of a sterile swab. If the lesion is open, as much of the superficial portion should be removed as is possible, and the specimen taken from the deeper part. If this is not done the specimen will usually be contaminated. All specimens taken on swabs must be protected from drying. This is best accomplished by placing the swab in a sterile test tube containing a drop or two of sterile salt solution. The swab, which is longer than the test tube, should be placed in the test tube in such a manner that the cotton pledget is just above the salt solution, but does not touch it. The cotton plug is inserted, and this holds the swab in place.

Smears for gonococci in the female should be taken from the meatus of the urethra and the cervix uteri. In acute gonorrhea in the male the smears are obtained from the urethra. In chronic cases in the male the material may be obtained by massaging the prostate and seminal vesicles. In children suspected of having gonorrheal vulvovaginitis, the smears and cultures are usually made from the vagina

because it is the vagina that is primarily attacked. It is not wise to rely on smears and cultures made from the external genitals; in some cases they have to be made from the cervix. A special technic for collecting the material must be carried out when making cultures for gonococci.

Cerebrospinal fluid is obtained by inserting a large needle into the vertebral canal. This procedure, known as *lumbar puncture*, is carried out as follows: after the overlying skin has been sterilized and anesthetized, the needle is introduced into the canal slightly to one side of the midline and between the third and fourth lumbar vertebrae. The removal of too much fluid may lead to serious results. The strictest asepsis should be observed and a sterile dressing should be placed over the site of puncture.

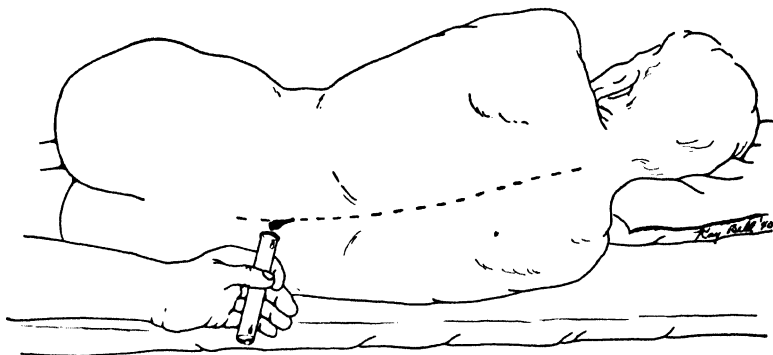


Fig. 50.—Patient undergoing lumbar puncture. Note position of needle and fluid dripping into container. (From Clendening and Hashinger: *Methods of Treatment*, The C. V. Mosby Co.)

Pleural and peritoneal fluids are obtained by inserting a needle through the wall of the chest or abdomen. After the needle has been introduced, the fluid is withdrawn by aspirating with a syringe or allowing it to drain into a sterile container. The strictest asepsis should be observed in puncturing the chest or abdominal wall.

Smears and cultures from the conjunctiva are made with swabs wet with sterile salt solution. Material from the eye should be handled in such a manner that injury will not be produced and infection will not be spread to adjacent parts or the other eye.

Questions for Review

1. What are two important facts which must be kept in mind when collecting specimens for bacteriological examination?
2. List the rules applicable to the collection of any specimen for bacteriological examination.
3. What special precautions should be taken in collecting urine specimens for bacteriological examination? Is it always necessary to catheterize the male?
4. How should the skin be prepared for the collection of a blood culture? Why is such a complicated procedure necessary?
5. What vein is usually used as a collection site for most blood specimens? How would you collect a blood specimen from an infant?
6. What are the precautions to be considered in collecting sputum specimens? In collecting stool specimens?
7. How would you handle a specimen of pus which is to be cultured?

References

(See References Chapter VIII.)

CHAPTER XI

REMOVAL OR DESTRUCTION OF BACTERIA BY MECHANICAL AND PHYSICAL MEANS

Sterilization is the process of destroying or removing all bacteria present. An object that has all bacteria upon or within it destroyed is said to be *sterile*. The length of time an object remains sterile depends on how well it is protected from bacteria after it is sterilized. For instance the outside of a tube of culture medium soon becomes nonsterile because it is in direct contact with the bacteria of the air, while the culture medium which is protected from bacteria by the cotton plug remains sterile indefinitely. Sterilization may be accomplished by mechanical, physical, or chemical means.

Removal or Destruction of Bacteria by Mechanical Means.—There are three chief mechanical methods of removing or destroying bacteria; namely, (1) scrubbing, (2) filtration, and (3) sedimentation.

Scrubbing is usually done with water to which some chemical agent, such as soap or sodium carbonate, has been added. The process is both mechanical and chemical. The process of scrubbing within itself removes many bacteria mechanically while the incorporated chemical acts on them chemically. Scrubbing with soap and water is of great importance, because on this process is based the ordinary conception of cleanliness. It finds its practical application in cleansing hands and person, floors, woodwork, clothing, etc.

Bacterial filtration is the process of passing a liquid containing bacteria through a material, the pores of which are so small that the bacteria are prevented from passing through. This renders the fluid sterile. This process is used in the laboratory for sterilizing liquids that cannot be heated and for the separation of toxins, enzymes, etc., from the bacteria that produce them. The materials most often used for bacterial filtration are unglazed porcelain, diatomaceous earth, and asbestos. The finest mesh filter paper

of the best quality will not hold back bacteria. Bacterial filters are so constructed that the material to be filtered is made to pass through a disk or the wall of a hollow tube made of the filtering material.

The water supply of a city is often purified by filtration. This is accomplished by allowing the water to pass through beds of gravel and sand with outlets at the bottom for the water to drain away. The process is partly mechanical and partly biological because the nearest approach to complete removal is not reached until a peculiar gelatinous scum forms over the filter bed. The exact mode of action of this scum is not known.

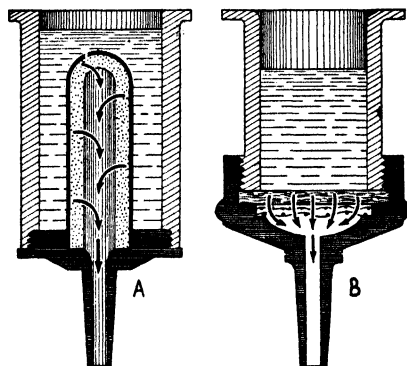


Fig. 51.—Bacterial filters. A, Berkefeld type of filter in which the material to be filtered is passed through the wall of a hollow cylinder. B, filter of the Seitz type in which the material to be filtered is passed through an asbestos disk. Filtration is brought about by suction. The arrows indicate where filtration takes place. (From Rice: *A Textbook of Bacteriology*. W. B. Saunders Co.)

Sedimentation is the process by which suspended particles settle to the bottom of a liquid. It finds practical application in the purification of water by natural or artificial means. In nature large particles and suspended bacteria sink to the bottom of water in lakes, ponds, and flowing streams. Sedimentation plays no inconsiderable part in the artificial purification of water. Here the water is held in large basins known as sedimentation basins, and the process is often accelerated by the addition of some coagulating agent such as alum. After sedimentation the water is filtered.

Sterilization by Physical Means.—The most widely applicable and effective sterilizing agent is heat. The temperature

which kills a twenty-four-hour liquid culture of a certain species of bacteria at a pH of 7 (neutral reaction) in ten minutes is known as the *thermal death point* of that species. Since this represents the temperature at which all bacteria are killed, it is obvious that many are destroyed before this temperature is reached. It is necessary that bacteria be in a neutral medium when their thermal death point is determined because they are more susceptible to heat if they

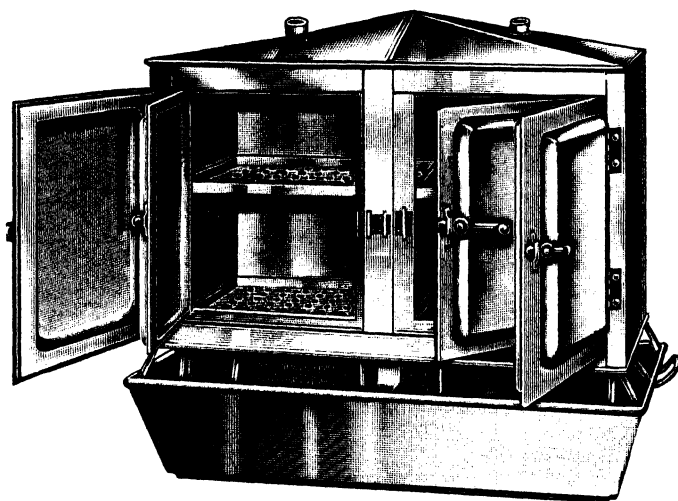


Fig. 52.—Arnold sterilizer. Water is poured in the bottom pan and the material to be sterilized is placed in the upper chambers. When the water is boiled, steam passes up through the perforated bottoms of the upper chambers and comes in contact with the material to be sterilized. (Courtesy Greene Bros., Dallas, Texas.)

are suspended in either a highly acid or a highly alkaline medium. Aside from burning, which is really a chemical process, heat may be applied in the form of *moist heat* or *dry heat*. Moist heat may be applied in the form of hot water or as steam. The most common method of sterilizing with hot water is by boiling. Boiling kills all vegetative bacteria in less than five minutes. Therefore, we can rest assured that all vegetative bacteria that come in contact with boiling water will be killed if the contact is continued for that time. It should be remembered that the interior of materials boiled may not be sterilized in that time because the heat may not penetrate the interior to any great degree until

the boiling has continued for a much longer time. Spores are much less quickly destroyed, but boiling for one or two hours usually suffices to destroy them. The addition of 1 per cent sodium carbonate to boiling water hastens the destruction of spores and prevents the rusting of instruments. The presence of organic material retards sterilization.

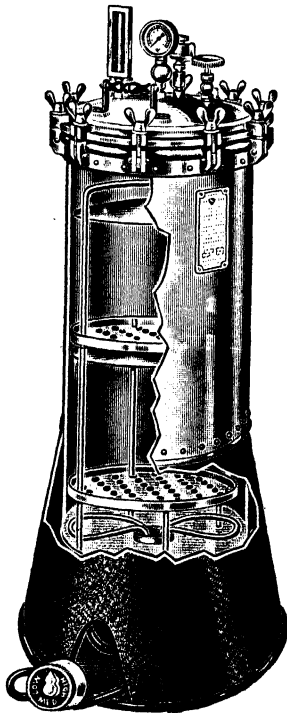


Fig. 53.—Vertical type of autoclave. The outer wall has been cut to give a view of the interior. Note rack for holding material to be sterilized and electric heating element at bottom. (Courtesy Greene Bros., Dallas, Texas.)

In the preparation of bacterial vaccines it is necessary to kill the bacteria at as low a temperature as possible because a temperature of more than 62° C. will coagulate the bacterial protein and render the vaccine worthless. It has been found that an exposure for one hour to a water-bath temperature of 60° C. will kill any of the ordinary bacteria used in making vaccines. Bacterial vaccines are sometimes sterilized by the addition of chemicals such as phenol, cresol, etc.

Steam may be applied as free-flowing steam or under pressure. Free-flowing steam has about the same sterilizing action as boiling water. Steam under pressure is the most powerful method of sterilizing that we possess. The process is carried out in an apparatus known as an autoclave which consists of a cylinder, one end of which is so constructed

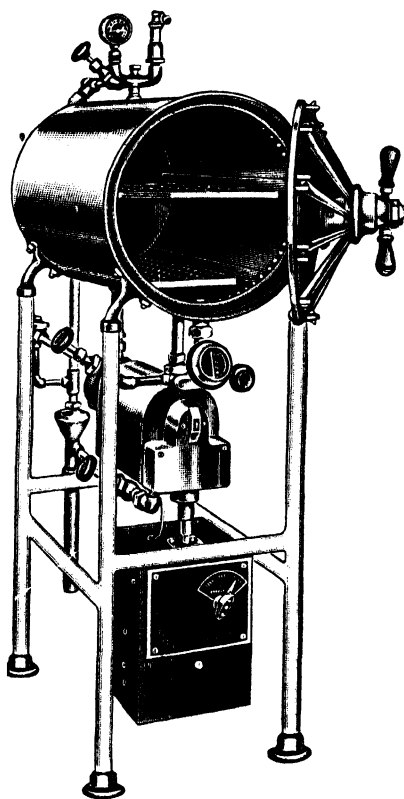


Fig. 54.—Horizontal type of autoclave. Note shelves for material to be sterilized and electric heating unit at bottom. (Courtesy Greene Bros., Dallas, Texas.)

that it may be opened to receive the material to be sterilized and then closed to make a steam-tight joint. In the vertical type of autoclave, water is placed in the bottom of the cylinder, while in the horizontal type the water is in a small tank below the cylinder and a pipe conveys the steam generated by heating the water to the sterilizing chamber.

Autoclaves are provided with safety valves which release the pressure when it reaches the point at which the valve is adjusted.

Steam under pressure is hotter than free-flowing steam and the higher the pressure the higher the temperature; for instance, while the temperature of free-flowing steam is 100°C ., it is 121°C . at 15 pounds pressure and 126°C . at 20 pounds pressure. Steam under a pressure of 15 or 20 pounds will kill all organisms and spores in fifteen minutes.

In operating an autoclave a vent must be left open so the air can escape as the temperature is raised. If this is not done air will be entrapped in the autoclave and the moisture content of the autoclave will be reduced and its sterilizing capacity lessened. This is because sterilization by heat is primarily a process of protein coagulation, and for protein coagulation to occur most easily, sufficient water must be present. After sterilization has proceeded the required length of time, the heat is cut off and the autoclave is allowed to cool. When a liquid is sterilized in the autoclave, it is heated above the boiling point but the increased pressure keeps the liquid from boiling. If the pressure is released rapidly, there will be violent boiling with wetting and blowing out of the plugs and loss of part of the liquid.

Since sterilization by steam under pressure is primarily a matter of temperature and the increase in pressure plays its part in the sterilizing process by increasing the temperature, the height to which the thermometer instead of the pressure gauge rises should be the guiding factor in the operation of the autoclave. This is particularly true because many pressure gauges are inaccurate. As a whole, inaccurate pressure gauges read too high. A thermometer placed at the bottom of the sterilizer is a better indicator of the efficiency of the sterilizing process than one placed at the top, because, if any part of the autoclave fails to receive the full benefit of the steam, it is the bottom part.

*Fractional Sterilization (Intermittent Sterilization).—*When certain materials, especially culture media, that cannot withstand the temperature of an autoclave are to be sterilized, the procedure known as fractional or intermit-

tent sterilization is used. This consists of exposing the material to free-flowing steam for thirty minutes on three successive days and storing it under conditions suitable for bacterial growth between times. At the first heating all vegetative bacteria are killed, but the spores are not affected. The material is then placed under conditions suitable for bacterial growth; the spores develop into vegetative bacteria and the second heating kills them. The second incubation and third heating are added to insure complete sterilization. This method of sterilization is of little value unless the material being sterilized is of such a nature as to promote the transformation of spores into vegetative organisms. It therefore finds its greatest field of usefulness in the sterilization of culture media. The low temperature method of sterilizing vaccines may be applied in a fractional manner to materials, such as serums, etc., that cannot withstand a temperature of 100° C. In other words, such materials may be sterilized by heating to a temperature of 55° to 60° C. for one hour on five or six successive days.

Dry heat (hot air) sterilization consists of baking the material to be sterilized in suitable ovens. Dry heat of a given temperature is not nearly as effective a sterilizing agent as moist heat of the same temperature. As has been explained, the less water present, the more difficult it is to coagulate proteins, and dry heat removes water from bacteria while moist heat adds water to them. Moist heat also has greater penetrating power than dry heat. For dry sterilization the temperature should be 160° C. for at least one hour. A temperature of more than 200° C. causes cotton and cloth to turn brown. A moderate degree of dry heat is injurious to most fabrics. Dry heat is used to sterilize glassware and articles that are injured by moisture. In dry heat sterilization the temperature should be slowly raised, and after sterilization is complete the oven should be allowed to cool slowly. This prevents breakage of glassware. There are two causes of ineffective dry heat sterilization: (1) too close packing of the material to be sterilized, and (2) irregular distribution of temperature within the sterilizer.

All objects that are of no value or cannot be used again should be burned.

Pasteurization is a special method of heating milk or other liquids to a mild degree of temperature for a short time. The purpose of pasteurization is to destroy non-spore-bearing pathogenic or other undesirable organisms without changing the composition of the material being sterilized. This method will be discussed further in the chapter on milk.

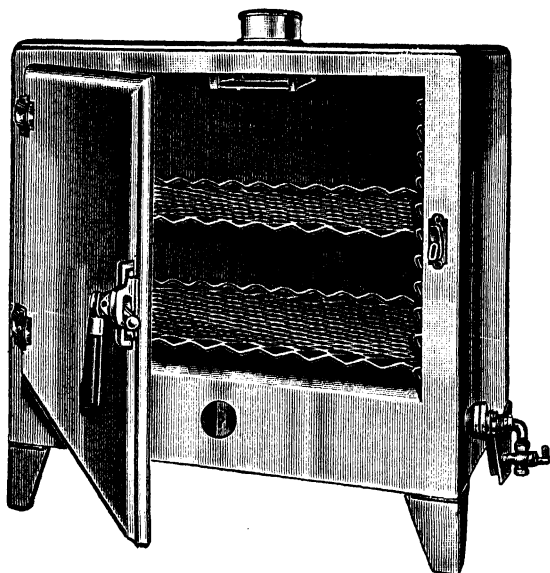


Fig. 55.—Dry air sterilizer; electrically heated. (Courtesy Greene Bros., Dallas, Texas.)

Natural Methods of Removing or Destroying Bacteria.—

If a culture of bacteria is dried, the majority of the bacteria are quickly killed, but some may live for a long time. Spores and encysted protozoa resist drying for a long time. Although drying is an important natural method of removing or destroying bacteria, it has little practical application to artificial sterilization except that sterile dressings, etc., should be kept dry. Sunlight has a marked inhibitory and destructive action on bacteria. It will kill *Myco. tuberculosis* within a few hours and will kill many other bacteria in a shorter time. Sunlight is Nature's great sterilizing agent.

but it is so irregular in its presence that it cannot be depended upon. The bacteria-destroying action of both drying and sunlight are taken advantage of in the home drying of food.

Questions for Review

1. Discuss fractional or intermittent sterilization.
2. Explain why moist heat is more effective than dry heat in the process of sterilization.

Completion Test

1. Three general methods of sterilization are _____, _____, and _____.
2. Bacterial filtration is a type of _____ sterilization.
3. The process of destroying or removing all bacteria is known as _____.
4. The temperature that kills a liquid culture of a certain species of bacteria in ten minutes is known as the _____ of that species.
5. The process by which suspended particles settle to the bottom is known as _____. This process is used in the purification of _____.
6. Moist heat may be applied in the form of _____ or as _____.
7. Boiling kills all vegetative bacteria in less than _____ minutes.
8. Spores may be killed by boiling for _____ hours.
9. Bacterial vaccines may be sterilized by adding chemicals such as _____ and _____.
10. _____ is the most powerful method of sterilization we possess.
11. Steam under pressure of _____ pounds or _____ pounds will kill all organisms in _____ minutes.
12. _____ is an important method of natural sterilization.

References

- Rosenau, Milton J.: Preventive Medicine and Hygiene, New York, 1935, D. Appleton-Century Co.
- McCullough, Ernest C.: Disinfection and Sterilization, Philadelphia, 1945, Lea & Febiger.
- Stitt, Clough, and Branham: Practical Bacteriology, Haematology and Parasitology, Philadelphia, 1948, P. Blakiston's Son and Co.
- Kolmer and Boerner: Approved Laboratory Technic, New York, 1945, D. Appleton-Century Co.
- Jordan, Edwin O., and Burrows, William: Textbook of Bacteriology, Philadelphia, 1945, W. B. Saunders Co.

CHAPTER XII

THE DESTRUCTION OF BACTERIA BY CHEMICALS

There are certain definitions with which the student must be familiar in order to understand this and the following chapters. As we have already learned, sterilization is the destruction or removal of all bacteria present. *Disinfection* is the destruction of all disease-producing organisms and their products. Disinfection does not take into consideration the saprophytic organisms present which may or may not be destroyed. Disinfection is usually accomplished by means of chemical agents known as *disinfectants*. *Germicides* or *bactericides* are chemicals that destroy bacteria. *Antiseptics* are agents that prevent the growth of bacteria but do not necessarily destroy them. *Asepsis* means the absence of microorganisms. In an aseptic operation, the field of operation, instruments, dressings, and hands of those taking part are rendered bacteria-free by sterilization and the operation is conducted in such a manner that it is kept bacteria-free, the purpose of all of which is to avoid infection of the patient. *Fumigation* is the liberation of fumes or gases for the purpose of destroying insects or small animals. *Deodorants* are substances or things that destroy or mask offensive odors. They may have neither disinfectant nor antiseptic action and may have a general tendency to obscure infectious material rather than to destroy it. *Bacteriostasis* refers to that condition in which bacteria are prevented from multiplying, but are in no other manner affected, by such agents as low temperature, weak antiseptics, dyes, etc. *Agents capable of causing bacteriostasis are known as bacteriostatic agents*. Antiseptics and chemical bacteriostatic agents are synonymous terms. *Preservatives* are antiseptics or bacteriostatic agents used to prevent the deterioration of foods, serums, vaccines, etc.

How Disinfectants Act.—Chemical disinfectants are of two types: (1) those such as bichloride of mercury which

coagulate bacterial proteins and (2) those which change the composition of a protein so that it no longer exists as such.

Qualities of a Good Disinfectant.—There are certain requirements which a chemical should meet before it is selected for general use as a disinfectant. At the present time no single disinfectant meets all of them. Important among these requirements are: (1) ability to form destructive chemical combinations with bacterial cells, (2) rapidity of action, (3) low toxicity for human tissue, (4) action not retarded by presence of organic matter, (5) ability to penetrate material being disinfected, (6) easily dissolved, (7) stability of composition, (8) absence of destructive action on material being sterilized, such as flesh, instruments, etc., (9) absence of unpleasant odor, and (10) easily obtained at comparatively low cost. *The most important feature of a disinfectant is its ability to form combinations with bacterial cells that are destructive to the bacteria.*

Factors Influencing the Action of Disinfectants.—The factors influencing the action of disinfectants may be classified as: (1) the qualities of the disinfectant, (2) the nature of the material to be disinfected, (3) the concentration of the disinfectant, and (4) the manner of application. A chemical in a solution of one strength may be a disinfectant, while in a weaker solution it may act only as an antiseptic, and in the case of certain very weak solutions may actually stimulate the growth of bacteria. The relative germicidal properties of the salts of a heavy metal are in proportion to their ionization. For instance, of the mercury salts, the bichloride is the most powerful germicide because it dissociates (ionizes) to a greater extent than the other salts. The material being disinfected should be considered from the following standpoints: (1) kind and number of bacteria present, (2) whether the bacteria are in the vegetative or spore form, (3) whether they are in clumps or in an even suspension, and (4) whether or not organic matter or chemicals that render the disinfectant inert are present. As a rule, the process of disinfection is a gradual one, and a few bacteria survive longer than the majority. To be success-

ful the disinfectant must be applied for a length of time sufficient to destroy these bacteria. An important factor relating to the application of a disinfectant is the temperature at which it is applied. The higher the temperature, the more active the disinfectant. It is important to remember that a disinfectant must penetrate all parts of the material being disinfected because it must actually come in contact with bacteria in order to destroy them and that to choose a disinfectant properly it must be chosen in accordance with the material to be disinfected.

Disinfectants other than the strong acids and alkalies are divided into several groups:

1. Metallic salts (salts of mercury, silver, copper, zinc, etc.).
2. Halogens (chlorine, hypochlorites, iodine, bromine, etc.).
3. Oxidizing agents (hydrogen peroxide and potassium permanganate).
4. Carbon compounds (phenol, creosote, salicylic acid, benzoic acid, thymol, alcohol, formaldehyde and volatile oils).
5. Miscellaneous (sulphurous acid, boric acid, etc.).

Standardization of Disinfectants and Antiseptics.—The disinfectant or antiseptic action of a chemical as compared with that of phenol (carbolic acid) acting for the same length of time on the same organism under identical conditions is known as the *phenol coefficient* of the chemical. If it has a coefficient greater than 1 it is a stronger disinfectant than phenol, and if it has a coefficient less than 1 it is a weaker disinfectant than phenol. In the Rideal-Walker method of determining the phenol coefficient, the action of the disinfectant is compared with that of pure phenol on typhoid bacilli.

The objections that have been raised against phenol coefficient methods are that they do not meet field conditions and that their results are not strictly comparable. In order to overcome some of these difficulties, the U. S. Department of Agriculture has devised the "wet filter paper method" and the "agar plate method." In the former, small squares of filter paper impregnated with *Staphylococcus aureus* are placed in the material to be tested for intervals of

five minutes, ten minutes, fifteen minutes, and one hour, after which they are placed in sterile broth and incubated for twenty-four hours.

In the "agar plate method," agar is melted and cooled to between 42 and 45° C., at which time it is inoculated with a culture of *Staphylococcus aureus* and poured into Petri dishes. After the agar has hardened, the substance to be tested is placed on the surface of the agar and the plates incubated for from twenty-four to forty-eight hours. If the substance inhibits the growth of the staphylococci, a zone without bacterial growth will be seen around the area where the substance is in contact with the agar.

I. Common Disinfectants and Antiseptics

There are myriads of cleansing and disinfecting chemicals and combinations, but it will be impossible to consider more than a few of the more important ones in this chapter.

Soap.—The major action of soap is the mechanical removal of bacteria brought about by scrubbing which is usually accompanied by the use of a generous supply of soap. Soap is destructive to a few bacteria because of its sodium and alkali content, but to remove effectively most bacteria, of which staphylococci, typhoid bacilli, and dysentery bacilli are examples, scrubbing must be followed by the application of alcohol or some other disinfectant. Organisms that are susceptible to the germicidal action of soap are pneumococci, streptococci, meningococci, and *Treponema pallida*. If soap is to be followed by some germicide, the soap should be washed off before the germicide is applied, because soap and germicide will often combine to form an inert compound. If soap is not properly handled and dispensed, it may within itself become a source of infection.

Bichloride of mercury (corrosive sublimate) is one of the best general disinfectants. A 1:2,000 to 1:500 solution will kill most vegetative bacteria within one to twenty minutes. A 1:500 solution kills most spores within one hour. The presence of albuminous materials, such as blood, pus, etc., inhibits its action because they combine with it to form inert albuminate of mercury. This may be prevented by

the addition of ammonium chloride, tartaric acid or citric acid. Such solutions are often used for disinfecting the hands or site of operation. The addition of sodium chloride will produce the same results but diminishes its germicidal value about one-half.

Bichloride of mercury is an odorless, very poisonous, white powder that irritates the skin and corrodes metals. Solutions should bear a poison label and should be colored with a dye. It cannot be kept in metal containers and cannot be used for sterilizing metal articles. It finds its greatest usefulness as a disinfectant for hands, glass, and rubber articles. On account of its irritant action on the skin, very strong solutions should not be used on the hands.

Mercuric iodide (biniodide of mercury) resembles bichloride in its germicidal action but is less irritating to the tissues and does not have such a tendency to tarnish metals as the bichloride. It is almost insoluble in water but this can be overcome by the addition of potassium iodide.

Mercurochrome is a combination of mercury and a derivative of fluorescein. A 2 per cent solution is used as a disinfectant of wounds. Stronger solutions are used as skin disinfectants. A 1 per cent solution is tolerated by the bladder and kidney pelvis.

Metaphen is an organic mercury compound that is said to be a more powerful germicide than bichloride of mercury. It may be used for sterilizing instruments and the skin, and to irrigate the urethra. It is used in strengths ranging from 1:10,000 to 1:1,000. It is said to be comparatively nontoxic, nonirritating, and nondestructive to metallic instruments and rubber goods.

Merthiolate is another organic mercury preparation. It is used for disinfecting instruments, the skin, and mucous membranes.

Mercresin is one of the newer germicides. It combines the germicidal action of the mercurials with that of the phenolic derivatives. It combines a maximum disinfectant action with a minimum of tissue injury. Its action is not inhibited by the presence of blood serum.

Alcohol is one of the most widely used disinfectants. Absolute alcohol has practically no germicidal action. Ninety-five per cent alcohol has some germicidal action and 50 to 70 per cent has the greatest germicidal value. The reason for this that alcohol acts by coagulation, and the presence of water is necessary for coagulation. The addition of alcohol to aqueous solutions of corrosive sublimate makes the latter more potent but reduces the disinfecting qualities of phenol and formaldehyde.

Boric acid is a weak antiseptic that is most often used as an eyewash.

Fuming nitric acid is the best agent for cauterizing the wounds inflicted by rabid animals.

Hydrogen peroxide owes its disinfecting qualities to the free oxygen that it liberates. It is a spectacular but not overly reliable antiseptic that deteriorates rapidly.

Sodium perborate is an oxidizing agent that is used in the treatment of trench mouth.

Silver nitrate has about one-half the germicidal action of bichloride of mercury on an aqueous suspension of bacteria, but if much albuminous material is present its germicidal action is equal to or even greater than that of bichloride of mercury. A 1:10,000 dilution inhibits the growth of bacteria. It has a selective action for gonococci. A 1 per cent solution is instilled into the eyes of newborn children to prevent ophthalmia neonatorum. The action of silver nitrate is retarded by chlorides, iodides, bromides, sulphates and organic matter. It is reduced on exposure to light and on account of its many incompatibilities should be used only in the presence of distilled water.

There are various unofficial salts of silver on the market such as colloidal iodides, albuminates and proteins that have fewer incompatibilities than silver nitrate. They have been used in various strengths with varying results.

Protargol and **neosilvol** are colloidal solutions of silver salts that are used on account of their nonirritating qualities.

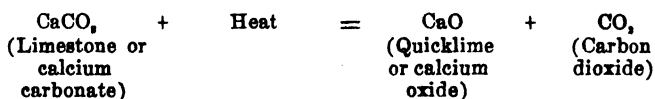
Copper sulphate is about one-half as effective a germicide as bichloride of mercury. Its chief value lies in its destructive action on the green algae which often grow in reservoirs

and render the water obnoxious. One part of copper sulphate per million parts of water will kill algae if the water does not contain an excess of organic matter. One part of copper sulphate added to 400,000 parts of water will destroy typhoid bacilli in twenty-four hours. It is not harmful to drink water that contains this amount of copper sulphate for a short time.

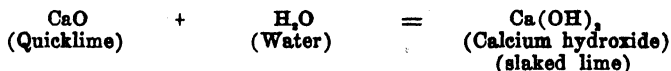
Ferrous sulphate (copperas) is usually used in the form of the impure commercial salt. In addition to being a good disinfectant, it is a good deodorant because it combines with both ammonia and hydrogen sulphide. It is an ideal disinfectant for use in damp musty places and around houses.

Potassium permanganate owes its action to its strong oxidizing qualities. Its action is weakened by the presence of organic matter. It has been used extensively in the treatment of infections of the genito-urinary tract.

Lime is one of the most common and, when properly used, one of the most effective germicidal agents. Limestone which occurs plentifully in nature is converted into *quicklime* by heating as shown in the following equation:



When quicklime is treated with one-half its weight of water, *slaked lime* is formed according to the following equation:



Slaked lime is a powerful disinfectant and is usually used in the form of "*milk of lime*" which is prepared by mixing one part of freshly slaked lime with four parts of water. Milk of lime is especially useful as a disinfectant for feces. A more dilute suspension of slaked lime is known as *white-wash*.

Lime preparations must not be exposed to the air because they combine with the carbon dioxide of the air to form calcium carbonate which is without antiseptic action.

Chlorine is widely used in the sterilization of drinking water, the purification of swimming pools, the treatment of sewage and the disinfection of wounds. It is applied by releasing the gas from cylinders or the use of compounds that liberate free chlorine. For sterilization to be effective the chlorine content of water must reach a concentration of 0.5 to 1 part per million parts of water.

Chlorinated lime (chloride of lime, bleaching powder, calcium hypochlorite) which is made by passing chlorine through freshly slaked lime is one of the most important of the chlorine liberating compounds used as disinfectants. It is most likely a definite but very unstable compound and its probable formula is CaOCl_2 . Its antiseptic action is due to the breaking down of calcium hypochlorite to hypochlorous acid which in turn decomposes with the liberation of chlorine and oxygen. A 0.5 to 1 per cent solution will kill most bacteria in from one to five minutes. A 1:100,000 solution will destroy typhoid bacilli in twenty-four hours. It bleaches and destroys fabrics and decomposes when exposed to the air. Chlorinated lime was formerly used extensively for disinfecting drinking water, swimming pools, etc., but in recent years it has to a great extent been replaced by chlorine gas. As a means of disinfecting excreta, chlorinated lime is probably without a rival. It has an advantage over bichloride of mercury in that its activity is not lessened to such a great extent by the presence of organic compounds and over phenol in efficiency and cost. On account of its oxidizing power it destroys the breeding place of germs as well as the germs themselves.

Dakin's solution is a neutral solution of sodium hypochlorite of between 0.45 and 0.5 per cent strength which was used extensively in World War I.

Compound solution of chlorine is made by adding hydrochloric acid to a solution of potassium chlorate and should contain 0.4 per cent of chlorine with some chlorine peroxide.

The *chloramines* are organic chlorine compounds that decompose slowly and liberate chlorine. They are used for the same purpose as Dakin's solution but have the advantage

that they act over a considerable length of time. The ones in most common use are chloramine-T and dichloramine-T.

Tincture of iodine is one of the best known and most widely used disinfectants for the skin, cuts, or wounds. Too strong solutions and very old solutions will burn the skin.

Phenol (carbolic acid) is a corrosive poison. A 1:1,000 solution inhibits the growth of bacteria. A 5 per cent solution will kill all vegetative bacteria and the less resistant spores in a short time. Contact with alcohol or ether decreases its action. The addition of from 5 to 10 per cent hydrochloric acid increases its efficiency. For woodwork, etc., the crude acid may be used because it is cheaper and more effective than the pure substance. Phenol is not greatly retarded in its action by the presence of organic matter. For this reason it is an excellent disinfectant for feces, blood, pus, sputum, and albuminous materials. It does not injure metals, fabrics, painted surfaces, etc. Its action is inhibited by the presence of soap. The crystals or strong solution should not be allowed to touch the skin. If this happens, alcohol should be applied at once. Dilute solutions should not be left in contact with the skin or mucous membrane for more than thirty minutes or an hour because they may cause necrosis.

Tricresol has a higher germicidal power than phenol but is less poisonous. *Liquor cresolis compositus* (U. S. P.) is an alkaline solution of cresol in soap. Similar but generally more expensive proprietary preparations are on the market. A 2.5 per cent solution of *liquor cresolis compositus* makes a good disinfectant for feces and sputum.

Sulphur dioxide is a gas formed by burning sulphur. It was formerly extensively used for house and room fumigation. Its germicidal action depends on the presence of moisture due to the fact that it combines with water to form sulphurous acid ($\text{H}_2\text{O} + \text{SO}_2 \rightarrow \text{H}_2\text{SO}_3$) which is really the destructive agent. It is injurious to fabrics and metals.

Formaldehyde is a gas which occurs in commerce as a solution of the gas in water. This solution is known as formalin and contains about 37 per cent of the gas. In ad-

dition to its disinfecting properties, it acts in some cases as a deodorizer and as a preservative. Its action depends on the presence of moisture, the concentration of the gas, the temperature, and the condition of the object to be sterilized. The presence of 1 per cent of the gas in a room or chamber will destroy all nonsporing pathogenic bacteria.

Chlorthymol, one of the newer preparations, is a powerful germicide, the action of which is not diminished by the presence of organic matter. It is prepared by making an alcoholic solution and diluting with water until the final product contains 0.2 per cent chlorthymol.

Dyes have lately come into use as antiseptics. Dyes such as gentian violet and crystal violet in high dilutions inhibit the growth of gram-positive bacteria but have little effect on gram-negative bacteria, while dyes such as acriflavine and proflavine inhibit the action of gram-negative bacteria but have little effect on gram-positive bacteria. The action of these dyes is made use of in obtaining pure cultures and in the treatment of infectious processes. Huddleson differentiated the three species of *Brucella* which cause undulant fever by their reactions to certain dyes. If it had not been for the advent of the sulfonamide drugs, the use of dyes as therapeutic agents would probably be much more highly developed than it is at the present time.

II. Treatment of Microbial Diseases With Chemicals

Although it is possible to treat many local infections with chemicals, the finding of a chemical which, when taken into the body by mouth or parenterally, will destroy microorganisms without injuring the body cells is a matter of difficulty. Examples of chemicals which will destroy microorganisms without injuring the body cells are quinine, atabrine, and plasmochin, which destroy the parasites of malaria, and arsphenamine and certain bismuth compounds which destroy the organisms of syphilis. Chaulmoogra oil has a similar but not so specific action on the leprosy bacillus.

Agents which destroy disease-producing microorganisms within the body without greatly affecting the cells of the body are known as *chemotherapeutic* agents. The treatment

of disease with chemotherapeutic agents is known as *chemotherapy*. Two chemotherapeutic agents of sufficient importance to merit separate consideration are the sulfonamide compounds and the antibiotics.

A. THE SULFONAMIDE COMPOUNDS

The sulfonamide compounds are compounds which contain the group— $\text{SO}_2\text{N}<$. Many of them are derived from the sulfonamide compound known as sulfanilamide. The following is a partial list of bacteria which respond to the sulfonamide compounds and the compounds to which they respond, enumerated in order of clinical value:

1. *Pneumococci*: (a) sulfadiazine, (b) sulfathiazole, (c) sulfapyridine.

2. *Hemolytic streptococci* (Lancefield's Group A): (a) sulfadiazine, (b) sulfanilamide, (c) sulfapyridine, (d) sulfathiazole.

3. *Gonococci*: (a) sulfathiazole, (b) sulfapyridine.

4. *Staphylococci*: sulfadiazine and sulfathiazole, apparently of about equal value.

5. *Meningococci*: (a) sulfadiazine, (b) other effective sulfonamides: sulfathiazole, sulfanilamide, sulfapyridine.

The method of action of the sulfonamide compounds is a matter concerning which there is much difference of opinion and a number of theories. The compounds cannot be considered sterilizing agents because they are not self-sterilizing. It seems reasonable to assume that they hold the bacteria in a state of inactivity until the defenses of the body rise sufficiently to destroy them. In addition to being used as general anti-infectives, the sulfonamide drugs may be used as local antiseptics in infected wounds, the abdominal cavity, and other parts of the body.

B. THE ANTIBIOTICS

Experiments and observations carried on during the last few years have proved that a number of organisms are capable of producing substances which have the power of inhibiting the multiplication of other organisms or even killing them. Such substances are known as *antibiotics*. As a rule.

antibiotics are more effective in their action against gram-positive bacteria than other organisms.

Tyrothricin.—The first antibiotic to be studied carefully was tyrothricin, which was isolated from an aerobic motile nonpathogenic bacillus growing in the soil. From tyrothricin were obtained two products—gramicidin (named in honor of the bacteriologist Gram) and tyrocidine. Both of these are highly antagonistic to gram-positive cocci. Tyrothricin is without effect when given by mouth and is a source of great danger when given parenterally. It therefore must be used locally only. It prevents bacterial growth and causes bacteria to undergo lysis.

Penicillin. —The next antibiotic to be discovered, and at the same time the most important one, is penicillin, which may be isolated from certain molds, the most important of which is *Penicillium notatum*. It is comparatively nontoxic, and may be administered intravenously, subcutaneously, in body cavities, by mouth, and locally. It is an effective agent against staphylococci, streptococci, pneumococci, meningococci, and other organisms. It does not have a great effect on gram-negative bacilli. Its use seems destined to revolutionize the treatment of syphilis. Just how penicillin acts is not known. Its action appears to be due to its effects on the bacteria themselves instead of stimulation of the defensive process of the host.

Streptomycin.—Streptomycin was isolated from *Streptomyces griseus*, an organism growing in the soil. Its action in a general way is like that of penicillin except that it is much more active against gram-negative and acid-fast bacilli. Like penicillin it may be administered by many routes.

Questions for Review

1. What lime compound is a good disinfectant? What precautions should be taken regarding the exposure of lime disinfectants to the air?
2. What is Dakin's solution? Give properties and use of the chloramines.
3. Discuss the treatment of bacterial diseases with chemicals.
4. Name four sulfonamide compounds used in medicine. Name some of the uses of penicillin.
5. Define chemotherapy; chemotherapeutic agent.

True-False Test

Place the word "true" or "false" before each statement.

- 1. Disinfection is the destruction of all disease-producing organisms and their products.
- 2. Antiseptics are agents that destroy bacteria.
- 3. Disinfectants and antiseptics are synonymous terms.
- 4. Asepsis means the absence of microorganisms.
- 5. Deodorants are substances or things that destroy or mask offensive odors.
- 6. Bichloride of mercury finds its greatest usefulness in sterilizing instruments.
- 7. The chief value of lime lies in its destruction of green algae which often grow in reservoirs and make the water obnoxious.

Completion Test

- 1. Factors influencing the action of disinfectants are -----, -----, -----, and -----.
- 2. ----- refers to that condition in which bacteria are prevented from multiplying.
- 3. Two types of chemical disinfectants are ----- and -----.
- 4. The higher the temperature, the ----- the disinfectant.
- 5. If a disinfectant or antiseptic has a phenol coefficient greater than 1, the disinfectant or antiseptic is ----- than phenol.
- 6. The major action of soap is the ----- removal of bacteria.
- 7. Organisms susceptible to the germicidal action of soap are -----, -----, -----, and -----.
- 8. The presence of albuminous materials such as blood, pus, etc., ----- the action of bichloride of mercury.
- 9. A 1:2000 to 1:5000 solution of bichloride of mercury will kill most vegetative bacteria within from ----- to ----- minutes.
- 10. ----- per cent alcohol has the greatest germicidal value.

References

- McCullough, Ernest C.: Disinfection and Sterilization, Philadelphia, 1945, Lea & Febiger.
- Rosenau, Milton J.: Preventive Medicine and Hygiene, New York, 1935, D. Appleton-Century Co.
- Jordan, Edwin O., and Burrows, William: Textbook of Bacteriology, Philadelphia, 1945, W. B. Saunders Co.

- Topley and Wilson: Principles of Bacteriology and Immunology, Baltimore, 1946, Williams & Wilkins Co.
- Spink, Wesley W.: Sulfanilamide and Related Compounds in General Practice, Chicago, 1942, Year Book Publishing Co.
- Kolmer, John A.: Penicillin Therapy, New York, 1947, D. Appleton-Century Co.
- Epstein and Williams: Miracles From Microbes, New Brunswick, 1946, Rutgers University Press.
- Huddleson, Forest: Brucellosis in Man and Animals, New York, 1939, The Commonwealth Fund.
- American Medical Association: New and Nonofficial Remedies.

CHAPTER XIII

PRACTICAL DISINFECTION AND STERILIZATION

I. Surgical Sterilization and Disinfection

Many different methods of sterilizing surgical instruments and supplies and of disinfecting wounds, the field of operation, and the hands of those taking part in surgical operations are used in different hospitals. In the following paragraphs no effort will be made to give all methods but only some of those most commonly used.

Instruments.—Nonecutting instruments may be sterilized by autoclaving at 18 pounds pressure (225° F.; 124° C.) for 30 minutes or by boiling 20 to 30 minutes. They must be completely submerged when boiling.

Boiling has a tendency to dull sharp edged instruments. Cutting instruments may be sterilized by submerging them in 1:1,000 metaphen, liquor cresolis compositus or 95 per cent alcohol for one hour. In some cases cutting instruments are sterilized by boiling for three to five minutes. In this case the cutting portion should be wrapped with cotton before boiling and the instruments should be kept from tossing around. This prevents dulling. The water should be boiling before the instruments are placed in it.

Surgical needles may be placed in packages and sterilized in the autoclave, or they may be placed in 95 per cent alcohol for thirty minutes and washed with sterile water.

Hypodermic Syringes and Needles.—Hypodermic syringes are most often sterilized by boiling in plain water for five minutes or by autoclaving. For certain purposes they are sterilized by dry heat (160° C. for one hour or more). Before sterilizing a hypodermic syringe the plunger and barrel should be separated or the plunger may be dipped in mineral oil and placed in the barrel. The latter method lengthens the period of usefulness of the syringe. Hypodermic needles may be sterilized by boiling, autoclaving, or by dry heat.

Dressings, Linens, Etc.—Towels, gowns, and other articles of cloth may be sterilized by autoclaving at 15 pounds pressure for 15 minutes. They should be arranged in packs $12 \times 12 \times 20$ inches in dimension, and wrapped in two layers of muslin or one layer of muslin and one or two layers of heavy paper.

Gloves.—When an operation is finished, the surgeon and his assistants should wash their gloves in cold water before removing them. After removal, the gloves are washed outside and inside with tincture of green soap, thoroughly rinsed and dried. They are then powdered, placed in glove envelopes and wrapped. They are sterilized as follows:

- a. Autoclave at 15 pounds pressure for 15 minutes.



Fig. 56.—A corner in the sterilizing room of a modern hospital. (Courtesy Parkland Hospital, Dallas, Texas.)

- b. Follow with vacuum for 5 to 10 minutes.
- c. Open door of sterilizer slightly and allow gloves to dry in sterilizer for about five minutes.
- d. Remove and separate packages to allow rapid cooling. This prevents sticking.

Caution: gloves are often ruined by being allowed to remain in the sterilizer too long.

Hand Brushes.—Boil for ten minutes and then place in 1:1,000 bichloride solution.

Sutures and Ligatures.—Tubes of suture material may be sterilized as follows:

- a. Scrub tubes with soap and water to remove greasy material.
- b. Rinse well with water to remove soap.
- c. Submerge in antiseptic solution (liquor cresolis compositus, 95 per cent alcohol or 1:1,000 metaphen) for one hour.
- d. Place in sterile suture jar containing one of the above antiseptics.
- e. Remove with sterile forceps and rinse in sterile water before using.

Silkworm-gut, silk, horsehair, and metal ligatures may be sterilized by boiling.

Water and Salt Solution.—Water and salt solution are placed in suitable containers and autoclaved at 15 pounds pressure for thirty minutes. Great care should be exercised to prevent fibers of lint or other particles from getting into solutions which are to be given intravenously.

Hard Rubber Goods.—Immerse in 5 per cent carbolic acid or in 1:5,000 bichloride solution for two hours; rinse with sterile water.

Soft Rubber Catheters.—Soft rubber catheters may be sterilized by boiling or autoclaving for 30 minutes. Repeated sterilization is injurious to the rubber.

Silk Catheters and Bougies.—Immerse in 1:1,000 mercuric cyanide or 1:1,000 bichloride of mercury for fifteen minutes. Rinse with sterile water before using.

Rubber Tubing for Intravenous Medication.—If new rubber tubing used in intravenous medication is not properly prepared, serious reactions may occur. The tubing should be of the best quality, and it should be treated in such a manner that all contaminating materials and the excess of sulphur, which is often present, are removed. The tubing is cut into lengths suitable for use and placed in a pan of 2 per cent sodium hydroxide where it is allowed to remain for twenty-four hours. It should be placed in the pan in

such a manner that the inside of the tubing is filled with the solution and no air bubbles are enclosed. At some period during the twenty-four hours the solution should be heated to almost the boiling point for a few minutes. The boiling removes the sulphur compounds. After this the tubing is attached to the water faucet and water is allowed to flow through it for three or four hours. It is then boiled in tap water and rinsed. After the tubing has received this preliminary treatment, it is used for intravenous medication only. After each intravenous injection tubing should be washed for thirty minutes by allowing tap water to flow through it, after which it is rinsed by allowing at least a liter of distilled water to run through it. Once done, the preliminary preparation need not be repeated. After the tubing has been prepared or cleaned, it is placed with the intravenous equipment and sterilized in the autoclave at 15 pounds pressure for 15 minutes. Proper preliminary preparation and thorough cleaning of rubber tubing subsequent to use will greatly reduce the number of reactions following intravenous medication.

Cystoscopes.—Immerse in 1:1,000 mercuric cyanide or 1:1,000 potassium mercuric iodide solution for fifteen minutes. Cystoscopes cannot be boiled because it will destroy them.

Hands.—There are many methods of disinfecting the hands. The following method gives good results:

- a. Wash hands and arms well with soap and water.
- b. With a sterile brush scrub nails and knuckles of both hands.
- c. Scrub hands beginning with thumb and in succession scrubbing the inner and outer surface of the thumb and fingers.
- d. Scrub palm and dorsum of hands and the forearm to two inches above elbow for three minutes.
- e. With a sterile orange stick clean under each nail thoroughly.
- f. With a second sterile brush scrub hands and arms in the same manner as with the first brush for seven minutes.

- g. Thoroughly rinse off all soap with water and then rinse hands in alcohol.
- h. With one end of a sterile towel dry one hand and with a circular motion dry the forearm to the elbow. With the other end of the towel dry the other hand in the same manner.

When scrubbing the hands for a surgical operation plenty of soap should be used and the scrubbing should be done with running water. When using cake soap, the soap is held between the brush and the palm until the scrubbing is complete. During the entire procedure the hands should be held higher than the elbows in order to prevent contamination.



Fig. 57.—Nurse scrubbing hands for surgical operation. (Courtesy Parkland Hospital, Dallas, Texas.)

Actual sterilization of the hands is usually not possible because bacteria live not only on the surface of the skin but also in its deeper layers and in the ducts of sweat glands and around the hair follicles. They are specially plentiful about the nails.

Site of Operation.—The deeper portions of the skin cannot be absolutely sterilized, but enough bacteria can be removed to cause infection to be an uncommon occurrence. The following outline represents a good method of skin preparation:

A. Preliminary Preparation (to be carried out several hours before operation):

- a. Shave part and wash thoroughly with tincture of green soap.
- b. Scrub with ether.
- c. Wash with alcohol.
- d. Cover with sterile towel and tape edges of towel to skin.

B. Preparation at Operation:

- a. Remove towel and place sterile towels above and below site to be prepared.
- b. Cleanse umbilicus with ether applicator.
- c. Scrub abdomen with ether, beginning with imaginary line of incision, working laterally and to bedline.
- d. Apply iodine to umbilicus with applicator.
- e. Paint abdomen with iodine on sponge. Begin at imaginary line of incision and proceed as in c.
- f. Remove iodine from around edges of field with an alcohol sponge.

Note I. Tincture of merthiolate (1:1,000) may be used instead of tincture of iodine.

Note II. In preparing any area for operation the imaginary line of incision is never painted with the same sponge more than once.

Note III. In case of emergency shave the field of operation and wash thoroughly with tincture of green soap, then proceed with "Preparation at Operation" as outlined above.

Operating Room.—One source of infection to which the operative field is exposed is pathogenic bacteria floating in the air. These arise from the noses and throats of the occupants of the operating room and may be destroyed by ultraviolet radiation.

Mucous Membranes.—Absolute sterilization of mucous membranes cannot be accomplished. The mouth and throat may be cleansed with Dobell's solution, hydrogen peroxide or hexylresorcinol. The vagina is swabbed with soap solution and then irrigated with 1:2,000 bichloride solution.

Wound Disinfection.—Wound disinfection is usually carried out by the use of one of the sulfonamide drugs, penicillin, chlorine disinfectants, or bacteria-inhibiting dyes. Strong disinfectants are no longer used. The sulfonamide drugs most commonly used are sulfanilamide, sulfathiazole, and sulfapyridine. Sometimes two are used in combination. They may be applied as dusting powders, in solution, in oily suspensions, or in the form of ointments. Ointments have a tendency to cause sensitization and should not be used for more than five days. Penicillin is applied in the form of powders, solutions, and creams. It is said to be the compound of choice in the treatment of wounds and burns infected with staphylococci. The chlorine disinfectants most often used are the chloramines. The dyes most often used are gentian violet, crystal violet, brilliant green, and malachite green because these dyes are effective against gram-positive organisms, which cause most wound infections. They have a moderately destructive action on tissue cells.

II. Disinfection of Excreta and Contaminated Materials From Infectious Diseases

It cannot be said that a case of communicable disease is being properly supervised until every avenue by which the infectious agent may be spread from the patient to others has been closed. These avenues cannot be said to be closed until all excreta and all objects that may convey the infection have been properly disinfected. A patient who is being cared for in such a manner that all avenues by which the infection may spread to others are closed is said to be *isolated*. A ward patient with a conscientious and capable nurse is more strictly isolated from the bacteriological point of view than is the patient in a room with plastered walls and airtight doors, provided the latter is attended by a careless or incompetent nurse. Isolation refers to avenues of

infection; not to walls and doors. Let it be remembered that bacteria are most pathogenic when first thrown off from the body.

Disinfection in infectious diseases is of two types: concurrent and terminal. By *concurrent disinfection* is meant the immediate disinfection of the excreta of the patient or objects that have become contaminated by the patient or his excreta. By *terminal disinfection* is meant the final disinfection of the room, its contents, and environs after the room has been vacated by the patient. The final chapter is written when patient and attendants have been proved not to harbor in their bodies the agent that caused the disease; that is, have not become carriers. In the following paragraphs will be given methods of disinfecting excreta, materials and objects by which infection is most often transmitted from the sick to the well.

The Hands of the Nurse.—Unless proper disinfection is carried out, the hands of nurses, doctors, or others that come in contact with the patient are almost sure to transfer the infectious agent to themselves or to others. Although the disinfection of the hands to prevent the spread of communicable diseases is not as time consuming as for a surgical operation, it should be just as conscientiously carried out. Washing the hands thoroughly with soap and warm running water is practical and, for most purposes, sufficient. In some hospitals a brush is used for scrubbing; in others the use of brushes is dispensed with. After washing, the hands should be rinsed and dried. This may be followed by rinsing in alcohol. The immediate use of a good hand lotion keeps the skin in good condition. The nails should be kept clean. Simply dipping the hand into an antiseptic is of little value. The hands should be disinfected every time they come in contact with the patient, before each meal, and when leaving the patient for the day. To allow the hands to come in contact with a person suffering from a communicable disease and then, without disinfecting, allowing them to come in contact with another person is little short of criminal neglect.

Soiled Clothing, Bed Linen, Etc.—All linens, clothing, etc., that have come in contact with the patient should be

considered contaminated and should be kept in the patient's room until ready for final disposal. In the hospital they may be wrapped in sheets or placed in pillow cases, after which they are put in a special bag, care being taken that the outside of the bag does not become contaminated. Before the bag is full, it is closed tightly, marked to indicate that it contains infectious material, and sent to the laundry. Upon reaching the laundry the bag is emptied into the washer, after which the bag itself is put in the washer. The washer is then closed and live steam introduced for from fifteen to twenty minutes. After this the regular procedure of the laundry is carried out. In the home the linen or bed clothing is bundled and carried to the kitchen or home laundry where it is placed in a boiler containing warm water and soapsuds and boiled for from ten to fifteen minutes. After boiling, the process of laundering may be completed in the home or by a commercial laundry. In some cases the boiler is carried to the patient's room to receive the soiled linen.

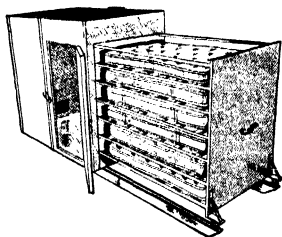


Fig. 58.—Sterilizer for mattresses and bed clothing. (Courtesy Ideal Mattress Co., Dallas, Texas.)

Mattresses, pillows, blankets, etc., may be sterilized by heat in special sterilizing chambers (Fig. 58) or they may be sterilized in a formaldehyde chamber.

Shoes.—Disinfection of shoes is of importance in "athlete's foot" and other fungus infections of the feet. Disinfection is best accomplished by placing a pledget of cotton saturated with formalin in each shoe and allowing the shoes to stay in a closed shoe box for twenty-four hours. In some cases, shoes are disinfected by spraying them with formalin from an atomizer for three successive evenings.

Feces and Urine.—Feces and urine, especially from patients with typhoid fever, should be mixed with either 5

per cent carbolic acid solution or milk of lime. The volume of disinfectant should be twice that of the material to be disinfected. Feces should be thoroughly broken up in order to insure penetration. After thoroughly mixing urine and feces with the disinfecting solution, the mixture should be allowed to stand for at least two hours before being emptied into the commode.

Discharges From the Mouth and Nose.—Discharges from the mouth and nose may be received on squares of tissue and placed in a paper bag pinned to the side of the bed. The bag may be disposed of by wrapping in several layers of clean newspaper and putting in the incinerator to be burned.

Sputum.—Sputum should not be allowed to dry in such a manner as to permit particles to float off in the air. It should be received in a paper cup held in a special metal holder. The paper cup is discarded and the metal holder sterilized by boiling at least twice daily (more often if necessary). To discard a paper cup remove the cup from the holder with forceps and set it on several thicknesses of newspaper. The cup is then filled with sawdust to decrease the amount of moisture and make the cup more easily burned. The paper is then wrapped around the cup and tied securely, after which the packet is placed in the incinerator or in a special receptacle to be carried to the incinerator later. After this has been done, the metal holder is boiled for ten minutes. Ambulatory patients often use collapsible cups.

Clinical Thermometers.—A clinical thermometer must be sterile each time it is used. After it is removed from the mouth and the temperature has been recorded, the thermometer is wiped with cotton and placed in 1:1,000 bichloride of mercury solution where it is allowed to remain for at least three minutes. Just before use wipe off with a piece of moistened cotton.

Eating Utensils.—A special covered container is placed in the sick room and the dishes are placed in the container, preferably by the patient himself. Care to prevent contamination of the outside of the container must be exercised. After the dishes, knives, forks, etc., are placed in the con-

tainer, they are carried to the kitchen and boiled in soapy water for five minutes. In some cases the eating utensils are carried to the kitchen before they are placed in the container. Leftover bits of food may be placed in a paper sack wrapped well with newspaper and placed in the incinerator. If this is not practical, the food remains may be placed in milk of lime or carbolic acid solution and left for one hour.

Terminal Disinfection.—Formerly it was the custom to fumigate all rooms with formaldehyde or sulphur dioxide after the removal of a patient suffering from a contagious disease. This is not being done so much now because it has been found that in many cases it is of little value or not necessary. It does have a definite value, however, in certain selected cases. When a patient is removed from a room the woodwork and furniture should be scrubbed with soapsuds and thoroughly aired. In some cases the scrubbing with soapsuds is followed by 1:1000 bichloride of mercury solution. After a few hours the dried mercury should be removed with water.

III. Disinfection of Articles for Public Use

Water Closets.—The bowls of water closets may be disinfected with crude carbolic acid solution. The woodwork and floors should be washed frequently with hot soapsuds solution.

The woodwork of schoolhouses, churches, theaters or other places of public assembly should be washed daily with soapsuds.

Public Conveyances.—All parts touched by the hands of passengers should be frequently washed with hot soapsuds solution.

IV. Fumigation of Rooms and Disinfection of Air

Fumigation.—In former years it was an almost universal procedure to put a sickroom "into fumigation" as soon as the room was vacated. Fumigation at that time meant terminal gaseous disinfection. Formaldehyde was the gas of choice and many elaborate pieces of apparatus for its use were on the market. This method of disinfection has to a great extent been abandoned, because formaldehyde does not kill

insects or small animals, and terminal gaseous disinfection of rooms was found to be of limited value because the causal agents of disease are transmitted by persons, animals, or insects instead of rooms, and these agents die rather rapidly under normal conditions. For instance, it is now known that the gaseous disinfection of rooms that have been occupied by patients with measles is of no value. Gaseous disinfection can be depended upon for surface disinfection only and is not dependable for the destruction of such organisms as *Myco. tuberculosis* and *C. diphtheriae*. The term *fumigation* now denotes the destruction of disease-carrying animals, insects, or vermin. The fumigant of choice is hydrocyanic acid. It is a deadly poison and must be handled with extreme care. Sulphur dioxide is a splendid insecticide, but because of its destructive action on metals and household goods it is seldom used in homes, public buildings, or hospitals.

Air Disinfection.—Two methods of destroying bacteria and other disease-producing agents as they are transferred through the air, which have lately come into use, are ultraviolet light and chemical disinfection. Ultraviolet light disinfection is being used with success in operating rooms, children's wards, and barracks. The method has a number of defects which remain to be overcome. Among these are irritation of the eyes and skin.

By chemical disinfection of the air is meant disinfection by chemical vapors liberated into the air. These chemicals are called *aerosols*. Two of the most effective aerosols are propylene glycol, which is effective in a dilution of one part in one hundred million parts of air, and triethylene glycol, which is effective when diluted to one part in four hundred million parts of air. The vapors may be introduced into rooms through ventilating systems, "bombs," or special equipment.

Questions for Review

1. What effect has boiling on cutting instruments? How may knives be sterilized?
2. Why must cystoscopes not be boiled?
3. Give a method of sterilizing the hands.
4. Give an emergency method of preparing the field of operation.
5. How may the air be kept free of pathogenic bacteria during the time of operation?

6. What is the difference between physical and bacteriological isolation?
7. How would you dispose of the feces and urine of a patient with typhoid fever?
8. Discuss the drugs used in wound disinfection.
9. Explain what is meant by concurrent disinfection and terminal disinfection.
10. What precaution should be taken in handling sputum from a patient with tuberculosis? How is sputum sterilized?
11. How are clinical thermometers kept sterile?
12. Briefly discuss terminal fumigation.
13. Briefly discuss the use of hydrocyanic acid as a fumigant.

References

(See also References Chapter XII.)

- Smith, Austin E.: Newer Concepts in the Prevention and Treatment of Wound Infections, J. A. M. A. 121: 851, 1943.
- Hart, Deryl: The Importance of Airborne Pathogenic Bacteria in the Operating Room, J. A. M. A. 117: 1610, 1940.

CHAPTER XIV

THE WORK OF USEFUL BACTERIA

Those in daily contact with bacterial diseases are likely to look upon bacteria as being only agents of harm, but such is not the case. *The majority of bacteria are helpful to man, animals, and plants, all of whom are dependent upon bacteria for their very existence* as will be shown in the following paragraphs. From a broad point of view it may be said that the disease-producing bacteria form a small and unimportant group.

Nothing gives us a better idea of the broad scope of bacterial activity than a consideration of the divisions of bacteriology, which are as follows:

1. *The bacteriology of Nature* which treats of the parts that bacteria play in the various processes of Nature.

2. *The bacteriology of disease* which treats of how and why bacteria cause disease.

3. *Sanitary bacteriology* which treats of the bacteriology of water supplies, sewage disposal, etc.

4. *Dairy bacteriology* which treats of the guarding of milk and milk products against organisms that cause disease or render milk or its products otherwise unfit for consumption. It also treats of the prevention of disease in cattle and the manufacture of certain kinds of milk and milk products.

5. *Food bacteriology* which treats of the prevention of the contamination of foods by harmful bacteria. It also treats of the methods used to manufacture certain foods, for example, vinegar, bread, etc.

6. *Industrial bacteriology* which treats of such processes as the curing of tobacco, retting of hemp, etc.

7. *Agricultural bacteriology* which in its wide sense includes dairy bacteriology and the bacteriology of domestic animals, but in its narrow sense refers to the bacteriology of the soil.

I. Bacteria in the Processes of Nature

Bacteria have been said to be Nature's garbage disposal system and fertilizer factory because they are the active agents in bringing about the decomposition of dead organic matter which releases the elements needed for the growth of plants and returns them to the soil. They decompose the wastes of man and animals. Bacteria purify sewage by living on the impurities of the sewage and converting them into in-offensive substances which serve as food material for plants. As the water trickles through the soil, bacteria may help remove its impurities so that though contaminated when it entered the earth, it may trickle out in a pure and uncontaminated state.

The chief elements entering into the bodies of animals and plants are nitrogen, carbon, hydrogen, and oxygen which are combined with other less common elements to form the complex substances known as proteins. Animals depend on plants for these elements. Plants receive their hydrogen and oxygen from water. The only form in which plants can assimilate carbon is as carbon dioxide. Carbon dioxide is present in the air in small quantities, and the supply must be constantly renewed. It is eliminated in the breath of all animals, because it is a waste product of animal life. If animals were sufficiently plentiful to eat all the plants and then converted all the carbon compounds of these plants into carbon dioxide and excreted it, the supply of plant food for animals and of carbon dioxide for plants would be perfectly balanced. Certain plant tissues, such as wood and cellulose, contain much carbon, but if eaten by animals they pass through the intestinal canal and are not broken down; therefore, their carbon is not converted into carbon dioxide and expired. Other plants die with much carbon present in their bodies. Much carbon is also present in the body tissues of animals when they die. It is seen that if there was not some method of recovering this carbon in a form available for plant growth (CO_2), plant life would soon cease and animals would have no food. Animal excreta, dead plants, and animal bodies are attacked by fungi and bacteria, and the process of decay begins. The complex

carbon compounds are attacked by one set of organisms and are broken down into carbon dioxide which floats away in the air to become plant food.

Nitrogen is one of the most important elements in the composition of the plant body. Nitrogen is abundant in the air but not in a form suitable for plant use. To be suitable for plant use, nitrogen must be in the form of nitrates. Since nitrates are present in the soil in very small amounts, they must be constantly renewed. The sources of nitrates are (1) from the decay of organic matter, and (2) the conversion of the nitrogen of the air into nitrates. Both of these processes are accomplished by bacteria. As has been previously noted, the decay of organic matter is brought about

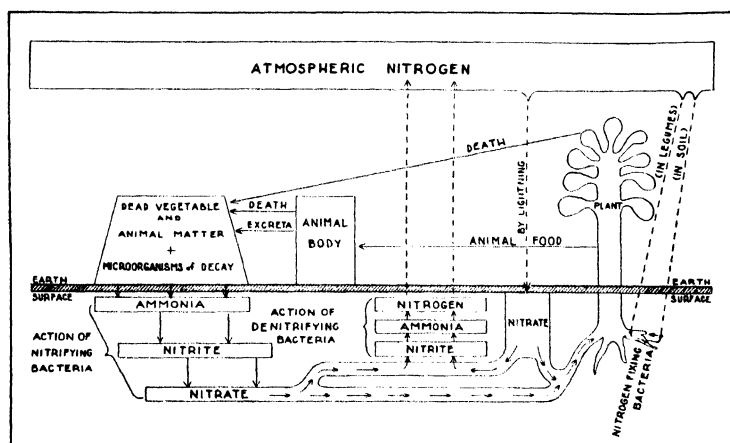


Fig. 59.—The nitrogen cycle. This diagram may best be understood by beginning with the collection of dead organic matter at the left. This has its origin from dead plants and the excreta and dead bodies of animals. The microorganisms of decay associated with the dead organic matter convert part of the organic matter into ammonia and the ammonia into nitrite, then the nitrite into nitrate. Added to this nitrate is the nitrate derived from the nitrogen of the air by the oxidizing action of lightning. Part of the nitrate from both sources is acted on by denitrifying bacteria and the remainder passes to the plant roots to be absorbed. That which is acted on by the denitrifying bacteria of the soil is converted step by step into nitrite, ammonia, and free nitrogen. The free nitrogen returns to the atmosphere. Another source of plant nitrogen is the nitrogen-fixing bacteria which remove nitrogen from the air and convert it into plant food. These bacteria are of two types: (a) those that live in the soil and (b) those that live in the root nodules of legumes. All that is definitely known about the action of these bacteria is given in the text. The above outline traces nitrogen from dead organic compound to living plant. Ultimately the plant will transfer its nitrogen to dead organic compound by dying or being eaten by some animal, the excreta and dead body of which becomes dead organic compound.

by different microorganisms which have various actions on it and many simpler compounds are formed. Among the first products formed by the breaking down of organic matter is ammonia. The ammonia is attacked by certain organisms known as *nitrifying* bacteria. One set of bacteria converts the ammonia into nitrites, and another set converts the nitrites into nitrates. These nitrates are absorbed by the plant roots and converted into complex nitrogen compounds like those with which we started.

Nitrogen fixation is the term applied to the recovery of free nitrogen from the air and its conversion into nitrates for the use of plants. This is accomplished by two groups of organisms. One group lives in the soil. The other group penetrates the root hairs and develops in the cells of the plant where they form nodules that become filled with the rapidly multiplying bacteria. These bacteria receive their nourishment from the plant and cause the nitrogen of the air to form a compound which is incorporated into the bacterial body. The plant removes these compounds from the bacterial body for its own use, and when it dies and decays the nitrogenous compounds are set free in the soil. Soils in which the products of decay are present are fertile. Those which do not contain them are not fertile.

II. Commercial Uses of Bacteria

Bacteria are variously used in the industries and arts. The following are some of the industries in which they are used:

1. Manufacture of Dairy Products.—Upon standing, milk undergoes souring due to the conversion of lactose (milk sugar) into lactic acid by bacterial action. This is known as “ripening.” Upon churning, the fat globules coalesce and take up a small amount of milk solids and water to form butter. The residue is known as “buttermilk.” The bacteria which play the most important part in ripening are the ordinary lactic acid bacteria which are normal inhabitants of milk. Ripening is often hastened by adding a culture of these bacteria. These cultures are known as “starters.” Originally the purpose of ripening was to preserve the milk until enough to churn had accumulated, but now its chief purpose is to give flavor to the butter.

Cheese consists of the curd of milk which is separated from the liquid portion by the action of the milk-curdling enzyme, rennin. After draining away the water, the curd is pressed into a block and partly dried. This is known as "green cheese." When green cheese is set aside for a time it undergoes changes which give it color, flavor and odor. This is known as "ripening," and is brought about by the action of enzymes in the curd, molds, yeasts and bacteria. The kind of cheese manufactured depends, to a great extent, on the kind of organisms that cause it to ripen.

One of the drinks which has grown popular during the past few years is "cultured buttermilk" of which there is more than one type. *Acidophilus milk* which is prepared by growing *Lactobacillus acidophilus* in milk is a pleasant drink and is said to possess considerable therapeutic value.

2. Manufacture of Alcoholic Beverages.—Alcoholic beverages are of two classes: those that are manufactured by fermentation alone, and those in which the alcohol is distilled off from the fermented mixture, thereby giving a product of higher alcoholic content than that of those manufactured by fermentation alone. Among the beverages that are manufactured by fermentation alone are wine and beer. Among those that are manufactured by distillation are commercial alcohol, whiskey and brandy. The manufacture of both fermented and distilled beverages depends primarily on the conversion of sugar into alcohol by yeasts. Wines are made by allowing grape juice to ferment. Beers are made from grains, most often barley. Grains do not contain sugar at first, but when their seeds germinate an enzyme known as diastase is produced and it converts the starch of the grain into sugar. Grain starch that has been converted into sugar is known as *malt*. Germination is usually brought about by soaking the grain in water. The sugar (maltose) in the malt is converted into alcohol by yeasts. The growth of foreign organisms in beer often gives it an undesirable taste. This is known as "disease" of beer.

Purification of alcoholic beverages by distillation depends on the fact that alcohol has a much lower boiling point than water, and when a fermented mixture is heated to a tem-

perature considerably below the boiling point of water, the alcohol distills over and leaves the water behind. Commercial alcohol and whiskey are usually made by distilling fermented grains. Brandy is made by distilling fermented fruits. Rum is made by distilling fermented cane juice.

3. Baking.—The basis of baking is the same as that of the manufacture of alcoholic beverages, i.e., the conversion of sugar into alcohol and carbon dioxide. The difference is that it is the carbon dioxide and not alcohol that plays the important role in baking. When yeasts are mixed with the dough and bring about the fermentation of the sugar present, the carbon dioxide thus produced riddles the dough with small holes, causing it to "rise." When the dough is baked the heat causes the carbon dioxide to expand and to be driven off. This leaves the bread light and spongy. Of course some sugar must be present or fermentation will not take place. In some cases sugar is added to the dough but as a rule dough contains a small amount of diastase which converts some of the starch of the dough into sugar.

4. Manufacture of Vinegar.—There are several methods of making vinegar; it may be made from wine, cider, or from grains that have undergone alcoholic fermentation. In most methods of vinegar manufacture the first step is the production of alcohol by fermentation, and the second step is the conversion of the alcohol formed into acetic acid. The first step differs in no manner from the production of alcohol for other purposes. When the alcoholic liquor is exposed to the air a film known as "mother of vinegar" which contains acetic acid bacteria forms on the surface. These bacteria convert alcohol into acetic acid according to the following formula:



If the process continues too long, the bacteria decompose the acetic acid into carbon dioxide and water and the vinegar loses some of its strength.

5. Sauerkraut.—Sauerkraut is finely shredded cabbage which has been allowed to ferment in brine formed by salt and the cabbage's own juice. The finely shredded cabbage is

placed in layers in a cask and salt sprinkled over each layer. The layers are packed closely together by superimposing a weight upon them. The salt extracts juice from the cabbage and the bacteria present convert the sugar of the juice into lactic acid which helps to give the kraut its peculiar flavor.

6. Tanning.—The first step in tanning is the removal of hair, which is usually done by soaking the hide in a solution of lime. It has been found that old solutions which contain many bacteria remove the hair more effectively than fresh ones which contain few bacteria. The second process is softening in which bacteria partially decompose the hides and thus soften them.

7. Curing of Tobacco.—When tobacco leaves are cured they undergo changes in texture and flavor, and take on a brown color. These changes are accompanied by a decrease in sugar, nicotine and water. The process is apparently one of oxidation brought about by fermentation.

8. Retting of Flax and Hemp.—In flax and hemp plants the fibers are closely bound to the wood and bark of the plant by a glue-like substance. When these fibers are separated from the bark and wood, the commercial products hemp and linen are obtained. This separation is accomplished by subjecting the plants to the action of bacteria that dissolve the glue-like substance.

Manufacture of Antibiotics.—Within the last few years the manufacture of antibiotics has become a major pharmaceutical activity. The basic materials used are cultures of molds or soil bacteria.

Other Commercial Uses of Bacteria.—In addition to the commercial uses of bacteria given above, the following may be mentioned.

1. Curing of coffee and tea.
2. Manufacture of vitamins.
3. Sewage disposal.

Questions for Review

1. What is the purpose of decay?
2. How is the supply of carbon dioxide for animals and plants conserved?
3. What causes the root nodules on certain plants?

4. What determines the fertility of soil?
5. List seven commercial uses of bacteria.
6. Give three chemical equations as follows:
 - a. The conversion of maltose into alcohol.
 - b. The conversion of lactose into lactic acid.
 - c. The conversion of alcohol into acetic acid.
7. What commercial procedures do the equations in question 6 represent?

True-False Test

Place the word "true" or "false" before each statement.

- 1. Bacteria have been said to be Nature's garbage disposal system.
- 2. The majority of bacteria are helpful to man.
- 3. Nitrogen in the air is in a form suitable for plant use.
- 4. Nitrogen fixation is the term applied to the recovery of free nitrogen from the air and its conversion into nitrates for the use of plants.
- 5. Bacteria have nothing to do with the formation of lactic acid in the souring of milk.
- 6. Alcoholic beverages are those which are made by fermentation alone, and those in which the alcohol is distilled off, from the fermented mixture.

References

- Prescott and Dunn: Industrial Microbiology, New York, 1940, McGraw-Hill Book Co., Inc.
- Cutler and Crump: Problems in Soil Microbiology, New York, 1935, Longmans, Green & Co.
- Smeeton, Mary A.: Practical Microbiology, New York, 1939, The Macmillan Co.

SECTION II

RELATION OF BACTERIA TO DISEASE

CHAPTER XV

BACTERIA AND DISEASE

When bacteria or certain other disease-producing agents enter the body of a person or animal, multiply and produce disease, an *infection* is said to exist and the host is said to be *infected*. A disease brought about in this manner is known as an *infectious* disease. Infection and contamination have different meanings because the latter refers to the mere presence of infectious material; for instance, the hands of the attending nurse or the dishes used by a patient with typhoid fever may become contaminated with typhoid bacilli but an infection does not exist. The mere presence of bacteria in the body does not mean infection because bacteria normally inhabit many parts of the body without invading the deeper tissues to produce disease. These bacteria constitute the normal flora of the body.

Source of the Bacteria Causing Infections.—The bacteria that cause infections fall into two classes: (1) those that are capable of causing disease in healthy persons and reach such persons directly or indirectly from animals or persons ill of the disease or from carriers and (2) those that enter the tissues as a result of injury or lowered resistance on the part of the recipient or, possibly in some cases, an increase in the virulence of the bacteria themselves. Bacteria belonging to the first group are the most important because it is to this group that the bacteria causing communicable diseases belong. To the second group belong those bacteria that normally inhabit the body but produce disease only under certain conditions and certain bacteria that are introduced into the body from the outside by wounds, injuries, etc. To the first type composing the second group belong such organisms as staphylococci that live in the skin

and infect stitch wounds to produce stitch abscesses; and streptococci that may normally live in the nose, throat, and sinuses but invade the deeper tissues to produce infection when the body resistance is lowered or the tissues are injured. An example of bacteria that are introduced into the body from the outside are the organisms of tetanus and gas gangrene which are normal inhabitants of the soil but produce serious disease when introduced into the body through punctures, crushing wounds, etc.

How Pathogenic Bacteria Reach the Body.—From the standpoint of the manner by which their causative agents reach the body, infectious diseases may be classified as communicable and noncommunicable. A *communicable* disease is one whose causative agent is directly or indirectly transmitted from host to host. Examples of such diseases are typhoid fever and tuberculosis. The host from which the infection is spread is usually of the same species as the recipient, but such is not necessarily the case. For instance, cattle may transmit tuberculosis and undulant fever to man. Disease due to bacteria that normally inhabit the body, only occasionally producing disease, are infectious but not communicable and the same is true of diseases due to bacteria, such as tetanus bacilli, that inhabit the soil and produce disease only when introduced into the body through abrasions or wounds. The term “contagious” is applied to diseases that are easily spread directly from person to person. This term is gradually falling into disuse.

From another standpoint infections are classified as exogenous and endogenous. *Exogenous* infections are those in which the causative agent reaches the body from the outside and enters the body through some of the portals of entry. An *endogenous* infection is one due to bacteria normally present in the body. As has been said already, endogenous infections occur when the defensive powers of the host are weakened or, for some reason, the virulence of the microorganism is increased.

In practically all civilized communities the sources of most communicable diseases are present. These sources are typical cases, unrecognized cases, and carriers. How the

causative agents are spread from source to victim will be more fully discussed in a subsequent chapter.

How Bacteria Enter the Body.—Bacteria gain entrance to the body by several avenues and each species usually has its own avenue of entrance. The avenue by which an organism gains access to the body is known as the *portal of entry* of the organism. A brief discussion of these portals follows:

Skin.—Most pathogenic organisms do not penetrate the unbroken skin, but some do. Staphylococci and some of the fungi are able to penetrate the hair follicles and cause disease in the deeper tissues. As soon as the superficial layers of the skin are destroyed, infection is easily accomplished.

Respiratory Apparatus.—Pulmonary tuberculosis, pneumonia, and influenza are contracted by way of the respiratory tract. While it is not definitely known, it is reasonable to believe that the viruses causing measles, smallpox, and German measles gain entrance to the body through the respiratory tract.

Digestive Tract.—Some of the most important pathogenic organisms gain entrance to the body by way of the digestive tract. In many cases food and drink are the vehicles by which they enter. Such organisms are typhoid and dysentery bacilli, cholera spirilla, and the amebas of dysentery. Tuberculosis of childhood is usually due to an infection by way of the digestive tract, caused by drinking the milk of tuberculous cows. The great majority of the pathogenic bacteria enter the body via the digestive tract or respiratory system.

The Genitourinary System.—Certain infections are acquired chiefly through the genitourinary system. Chief among these are the agents causing the “venereal” diseases. Rarely other infections are acquired by this route.

Placenta.—Most organisms do not pass through the placenta but the organisms of syphilis and the smallpox virus may be so transmitted.

Factors Influencing the Occurrence of Infection.—The fact that bacteria have entered the body in no manner indicates that infection has occurred. Whether infection will occur or not depends on (1) the avenue by which the bacteria enter, (2) the virulence of the bacteria, (3) the number of bacteria, and (4) the defensive powers of the host. The relation of the defensive powers of the host to infection will be discussed in the next chapter.

Most pathogenic bacteria have definite portals by which they enter the body and fail to produce disease when introduced into the body by some other route. For instance, typhoid bacilli produce typhoid fever when swallowed but only a slight local inflammation when rubbed on the abraded skin, while streptococci produce an intense inflammation when rubbed on the skin and are without effect when swallowed. A few bacteria, however, for instance, streptococci and *Pasteurella tularensis*, the causative agent of tularemia, are able to enter the body by several different routes and in many cases the route by which the organisms enter the body determines the type of disease process brought about. For instance, when streptococci enter the body through the skin, they may cause a localized abscess (boil) or a septicemia, while upon entering the body through the lungs they may cause a streptococcus pneumonia.

If only a few bacteria enter the body they are likely to be overcome by the local defenses of the host even though the bacteria are of high virulence. Therefore, for infection to occur enough bacteria to overcome the local defenses of the host must enter the body.

By *virulence* is meant the ability of bacteria to overcome the defensive powers of the host and produce their pathogenic effects. Not only is there a difference in virulence among species but among members of the same species derived from different sources. As a rule, bacteria are most virulent when freshly discharged from the body of a person ill of the disease that they cause. Virulence may be increased by rapid transfer through a series of susceptible animals, allowing each animal to become ill, isolating the organisms from its excreta, and transferring them to a well

animal. An organism or disease-producing agent which is highly virulent for one species of animals and less virulent for another may, upon repeated passage through the animal for which it is less virulent, have a transposal of virulence, i.e., it becomes less virulent for the animal for which it was originally highly virulent, and highly virulent for the animal for which it was originally less virulent. Advantage is taken of this characteristic in the production of antirabic vaccine. Organisms harbored by carriers are usually of comparatively low virulence. Organisms whose virulence is decreased are said to be *attenuated*. Organisms often become attenuated when grown on artificial culture media, and the longer so grown, the greater the attenuation. The occurrence of epidemics has been explained by assuming that the causative organism of the disease becoming epidemic has, by repeated passage from person to person, become so virulent that everyone with whom it comes in contact is made ill.

How Bacteria Cause Disease.—When pathogenic bacteria enter the body, two opposing forces are set into action: one on the part of the bacteria whereby they strive to invade the tissues, multiply, and produce disease; and the other on the part of the body whereby it strives to prevent the invasion of the bacteria, destroy them, and cast them off. If the body wins the contest, the bacteria are destroyed and the body suffers no ill effects. If the bacteria win the contest, infection occurs and disease is produced.

Bacteria cause disease in several different ways. In some cases disease is due to the mechanical effects of bacteria, but in most cases it is due to the action of their toxins (see page 90). Both bacteria and toxins have a distinct tendency to attack certain parts of the body. For instance, typhoid bacilli attack lymphoid tissue, particularly that of the intestines; pneumococci most often attack the lungs; meningococci attack the meninges; tetanus toxin attacks the central nervous system; and diphtheria toxin exerts its action on muscles, nerves, and heart. This is known as *elective localization*.

Among the mechanical effects of bacteria are plugging of tissue spaces and capillaries by the bacterial cells.

Local Effects of Bacteria.—By local effects of bacteria is meant the changes produced in the tissues in which the bacteria are multiplying. The most prominent of these local effects is inflammation, the purpose of which is to destroy bacteria and prevent them from spreading widely. In infections such as typhoid fever and diphtheria the presence of the bacilli causes extensive necrosis which leads to sloughing and ulceration. Tubercles and gummas are localized overgrowths of tissue brought about by the presence of the organisms of tuberculosis and syphilis, respectively.

General Effects of Bacteria.—One of the most important general effects of bacterial infection is fever. In a general way the degree of fever indicates the severity of the infection except in overwhelming infections in which fever may be slight or absent.

A very common effect of infection is a change in the total number of leucocytes (white blood cells) and the relative proportion of the different kinds of leucocytes. This is why total leucocyte and differential counts are of such importance in the diagnosis of disease. In most infections the total number of leucocytes is increased. In some the number is decreased and in a few it is unchanged. Anemia is often a result of prolonged and severe infections. A most important result of infection, which often protects the host from subsequent infections with the same disease agent, is antibody production, which will be discussed in the next chapter.

Incubation Period.—When bacteria or certain other disease-producing agents invade the body, a variable length of time elapses before the manifestations of disease appear. This is known as the *incubation time* or *period of incubation*. The length of the period of incubation depends on several factors, among which are: (1) the nature of the disease-producing agent; for example, the incubation period of diphtheria is less than that of rabies, (2) the virulence of the agent, (3) the resistance of the body invaded, (4) the distance from the site of entrance to the focus of action; for instance, the incubation period of tetanus and rabies both of which exert their action on the brain is shorter

when the site of infection is about the face, and (5) the amount of the infectious agent that invades the body.

Types of Infection Produced by Bacteria.—A *local* infection is one in which the bacteria remain confined to a particular locality (example—boils and abscesses). A *general* infection is one in which bacteria or their products are spread generally over the body by the blood or lymph circulation. A *mixed* infection is one due to two or more organisms. If a person is infected with an organism and then becomes infected with another organism or organisms the latter infection is known as a *secondary* infection; the former is known as a *primary* infection. Secondary infections of the skin and respiratory tract are quite common and in some cases the secondary infection is more dangerous than the primary. An example of such dangerous secondary infections is the streptococcus bronchopneumonia that often follows measles, influenza, whooping cough, etc. Secondary infections are usually due to a lowering of the body resistance brought about by the primary infection. A *focal* infection is an infection confined to a restricted area from which infectious material spreads to other parts of the body. Examples of focal infections are infections of the teeth, sinuses, and prostate.

When bacteria enter the blood stream but do not multiply, the condition is spoken of as a *bacteriemia*. If they enter the blood stream and multiply, causing infection of the blood stream itself, the condition is spoken of as *septicemia*. Septicemia is the condition that the layman refers to when he speaks of "blood-poisoning." When the bacteria in the blood stream are spread to different parts of the body where they lodge and set up new foci of disease, the condition is called *pyemia*. When the toxins liberated by bacteria enter the blood stream and cause disease, the condition is spoken of as *toxemia*. Diphtheria is a good example of a toxemia. Saprophytic bacteria may grow on dead tissue, such as a retained placenta or a gangrenous limb, and produce poisons which cause disease when absorbed into the body. This condition is known as *sapremia*. Patients with chronic wasting diseases like cancer often die

from the immediate effects of some bacterial infection, especially streptococcus and pneumococcus infections. These are known as *terminal* infections.

An *endemic* disease is one that is constantly to a greater or less degree present in a community. When a disease attacks a large number of persons in a community in a short time an *epidemic* is said to exist. Endemic diseases may become epidemic. When a disease becomes epidemic in a great number of countries at the same time, it is said to be *pandemic*. A *sporadic* disease is one in which a case occasionally occurs in a community.

How Bacteria Are Thrown Off From the Body.—Just as they have definite avenues by which they enter the body, pathogenic bacteria have rather definite routes of discharge from the body which, to a great extent, depend on the part of the body that is the site of disease. The following outline gives the most important routes by which bacteria are discharged from the body:

1. **Feces**—Organisms of typhoid fever, paratyphoid fever, bacillary and amebic dysentery, cholera, and tuberculosis.
2. **Urine**—Organisms of typhoid fever, paratyphoid fever, tuberculosis (when affecting the genitourinary tract), and undulant fever.
3. **Discharges From the Mouth, Nose, and Respiratory Passages**—Organisms of tuberculosis, whooping cough, pneumonia, influenza, scarlet fever, and meningitis; viruses of measles, smallpox, mumps, poliomyelitis, and epidemic encephalitis.
4. **Saliva**—Causative agent of rabies.
5. **Blood (removed by insect bites)**—Organisms of malaria and tularemia; virus of yellow fever, *Rickettsiae* of typhus fever, and Rocky Mountain spotted fever.

Koch's Postulates.—Absolute proof that an organism is the cause of a given disease rests on the fulfillment of certain requirements which are known as "Koch's postulates." These postulates are as follows:

1. The organism must be observed in every case of the disease.

2. The organism must be isolated and grown in pure culture.
3. The organism must, when inoculated into a susceptible animal, give the disease.
4. The organism must be observed and recovered from the animal.

In many cases, however, an organism must be accepted as the cause of a disease without it fulfilling all of these requirements. For instance, the bacillus that causes leprosy has never been grown outside the human body.

Questions for Review

1. Discuss four factors influencing the occurrence of infection.
2. List four factors that determine the length of the incubation period.
3. State Koch's postulates.
4. Is an organism ever accepted as the cause of disease without its fulfilling all of Koch's postulates? If so, give an example.

True-False Test

Place the word "true" or "false" before each statement.

- 1. Infection refers to the mere presence of infectious material.
- 2. Bacteria that cause infections fall into two classes.
- 3. The host from which an infection is spread is always of the same species as the one infected.
- 4. Typhoid fever and tuberculosis are both infectious diseases.
- 5. Organisms of syphilis and the virus of smallpox may pass through the placenta.
- 6. By virulence is meant the ability of bacteria to overcome the defensive powers of the host and produce their pathogenic effects.
- 7. Bacterial toxins are not selective in action; that is, they do not have a distinct tendency to attack certain parts of the body.
- 8. The occurrence of epidemics is explained by the increasing virulence of the organism brought about by repeated passage from person to person.
- 9. Inflammation is an effort to retard the spread of infection.

Completion Test

1. When bacteria or certain other disease-producing agents enter the body of a person or animal, multiply, and produce disease, an ----- is said to exist

2. ----- infections are those in which the causative agent reaches the body from the outside and enters the body through some of the portals of entry.
3. An ----- infection is one due to bacteria normally present in the body.
4. Bacteria may enter the body by several avenues such as -----, -----, -----, and -----.
5. Organisms whose virulence is decreased are said to be -----.
6. The ----- is the length of time that elapses from the time the disease-producing agents invade the body until the manifestations of the disease appear.
7. A ----- infection is one in which the bacteria remain confined to a particular locality (ex. boils and abscesses).
8. A ----- infection is one in which bacteria or their products are spread generally over the body by the blood or lymph circulation.
9. A ----- infection is one due to two or more organisms.
10. If a person is infected with an organism and then becomes infected with another organism or organisms, the latter infection is known as a ----- infection; the former, as a ----- infection.
11. When bacteria enter the blood stream but do not multiply, the condition is spoken of as a -----.
12. If bacteria enter the blood stream and multiply, causing an infection of the blood stream itself, the condition is spoken of as -----.
13. When bacteria in the blood stream are spread to different parts of the body where they lodge and set up new foci of disease, the condition is known as -----.
14. When the toxins liberated by bacteria enter the blood stream and cause disease, the condition is spoken of as -----.

References

- Rosenau, Milton J.: *Preventive Medicine and Hygiene*, New York, 1935, D. Appleton-Century Co.
- Zinsser and Bayne-Jones: *Textbook of Bacteriology*, New York, 1939, D. Appleton-Century Co.
- Topley and Wilson: *Principles of Bacteriology and Immunology*, Baltimore, 1946, Williams & Wilkins Co.
- Boyd, Mark F.: *Preventive Medicine*, Philadelphia, 1945, W. B. Saunders Co.

CHAPTER XVI

DEFENSES OF THE BODY AGAINST INFECTION. IMMUNITY

If infection occurred each time infectious agents entered our bodies we would be constantly ill. In addition to the mechanical, chemical, and purely physiological defenses, discussed in another chapter (see Pathology, Chapter XXXIX), the body possesses defenses by which infectious agents may be destroyed even after they have entered the tissues. These defenses render the body resistant to some infections and immune to others. Immunity is an especially highly developed state of resistance.

Immunity Defined.—Before attempting a definition of immunity I shall give three examples. First: man does not contract many diseases common to lower animals because he is naturally immune to these diseases and many of the lower animals do not contract the diseases of man for the same reason. Second: if a person has measles, smallpox, or typhoid fever, the disease is rather severe for a time, after which recovery occurs and the person will not contract the disease again though repeatedly exposed to it; i.e., he has developed a permanent immunity to it. Third: if a horse is given frequent injections of diphtheria toxin, beginning with a small dose and gradually increasing the amount given at each injection, the horse will eventually be able to withstand thousands of times the amount of toxin required to kill an untreated horse; i.e., the horse has become immune to the action of diphtheria toxin. With these illustrations as a background *we may then define immunity, in the narrow sense, as a resistance possessed by an animal to infection with viruses, animal or vegetable parasites, or their products which are pathogenic for other animals of the same or different species.* Susceptibility is the reverse of immunity and is due to an absence or suppression of the factors that produce immunity. For instance, man is naturally highly susceptible to influenza, smallpox, and measles; moderately sus-

ceptible to rabies, tuberculosis, diphtheria, and pneumonia; and slightly susceptible to epidemic encephalitis, poliomyelitis and epidemic meningitis. Of course he may naturally (by having the disease) or artificially (by being vaccinated) acquire an immunity against many of the diseases to which he is naturally susceptible.

Immunity-Producing Diseases.—Among the diseases whose attacks usually confer a lasting immunity are typhoid fever, yellow fever, whooping cough, smallpox, measles, mumps, poliomyelitis, plague, scarlet fever, and tularemia. In both tuberculosis and syphilis the patient develops a considerable degree of immunity but if completely cured is as susceptible as ever.

A slight degree of immunity of short duration follows influenza, pneumonia, gonorrhea, staphylococcus infections, and streptococcus infections (except scarlet fever in which the immunity is permanent). In some patients an attack of erysipelas may actually render the patient more susceptible to subsequent attacks. The same was once thought to be true of pneumonia, but this view has been disproved.

The Two Theories of Immunity.—With the development of the science of immunology two schools of immunologists arose. The German school led by Ehrlich believed that the establishment of immunity was due to the development in the body fluids, especially in the blood, of certain substances known as “antibodies” or “immune bodies” which have the capacity to destroy invading disease-producing agents. This is known as the *humoral or chemical* theory of immunity. The French school of immunologists headed by Metchnikoff believed that the whole process of immunity was due to the ingestion and destruction of invading disease-producing agents by the leucocytes and certain other body cells. This is known as the *phagocytic or cellular* theory of immunity. These theories were once held as opposing theories, but they are not so considered now because it has been found that, to some degree, one process depends on the other, and that in some diseases both processes are very active, while in others one may take the leading rôle. Some diseases do not seem to stimulate any activity on the part of either; i.e.,

they are not followed by a condition of immunity. In the following paragraphs immunity due to antibody formation and immunity due to phagocytosis will be discussed separately, but this is done for the purpose of clarity only and should not be construed as indicating that they are separate processes.

I. Immunity Due to Antibody Formation

When a person or animal becomes immune to a disease, by having it or being vaccinated against it, the immunity is to a great extent due to the development within the body of substances that are capable of destroying the causative agent of the disease should it gain access to the body at a later time. These substances are known as "*antibodies*" or "*immune bodies*" and are produced by the body cells in response to the stimulating effect exerted upon them by the infection or vaccination. Bacteria and their products are not the only substances that stimulate the body cells to antibody production when introduced into the body. Other substances that are capable of causing the production of antibodies, when introduced into the body, are certain vegetable poisons, snake venoms and the red blood cells, blood serum, and other proteins of an alien species. A substance, such as any of these, that is capable of giving rise to the production of antibodies against itself when introduced into the animal body is known as an *antigen*. Antigens are of a protein nature. Carbohydrates and nonprotein substances are nonantigenic. The antigen-antibody reaction is specific; i.e., a given antigen promotes the production of antibodies only against itself and a given antibody acts only against the antigen that promoted its development. For instance, a person vaccinated against smallpox or typhoid fever is protected against smallpox or typhoid fever only, and the blood serum of a rabbit that has been repeatedly injected with the red blood cells of a sheep acquires the property of dissolving the red blood cells of sheep but not those of other animals.

Much is yet to be learned about the true nature of antibodies. They are intimately associated with the globulin fraction of the blood plasma. Many workers believe that the

globulin-producing cells of the body respond to the presence of an antigen in such a manner that not only ordinary globulin, but also a special type of globulin is produced and that this globulin is the true antibody. It is assumed that this globulin enters into some kind of chemical combination with the antigen when it again enters the body. Antibodies have not been separated from the blood in anything like a pure condition, and there are no ordinary physical or chemical tests for their identification. Therefore they are detected only by their action. Depending on their action, antibodies are classified as (1) antitoxins, (2) bacteriolysins, (3) agglutinins, (4) precipitins, and (5) opsonins. Many observers believe that all of these activities are produced by the same antibody, the nature of the activity depending on the conditions under which it takes place.

Ehrlich's Side-Chain Theory of Antibody Production.—

Although it has not been scientifically proved and is probably of greater historical than practical importance, Ehrlich's "side-chain theory" of antibody production has been more productive of research than any other. This theory assumes that the cell consists of a complex central nucleus of atoms to which are attached a number of simpler groups of atoms known as "side-chains" or "receptors" which combine with foods, toxins, and other antigenic substances. The theory further assumes that an antigen cannot combine with a cell that does not possess receptors for that particular antigen and that a cell may have specific receptors for many different antigens. If sufficient toxin or other injurious agent combines with the receptors of a cell, the cell is destroyed. If a smaller amount combines with the receptors, the receptors are destroyed, but the central nucleus retains its vitality. In this case the central nucleus begins to reproduce receptors to replace those destroyed and does not stop when the original number of receptors has been replaced but produces such an excess that some cannot remain attached to the cell and are thrown off into the blood and body fluids. These cast-off receptors are known as "antibodies." When the antigen that promoted the development of these antibodies again invades the body the antibodies combine with it and render it inactive before it has an opportunity to attack

the body cells. The antibodies thus render the body immune to the disease by protecting its cells against the disease-producing material. It should be understood that the nucleus spoken of in the preceding sentences represents a complex chemical combination and has no relation to the morphological nucleus of the cell, nor are there any microscopic structures of the cell corresponding to side chains.



Fig. 60.—Bleeding guinea pig from the heart. The blood serum of this little animal is particularly rich in complement. Guinea pigs may be bled every three or four weeks without injuring them. Note that the animal is anesthetized while being bled.

Complement.—Although complement is not an antibody it is discussed here because its presence is necessary for the complete action of certain antibodies, notably bacteriolysins and other cytolysins, and complement or a complement-like substance enhances the action of opsonins. Complement is a component of fresh blood serum and is not increased by im-

munization. There is considerable evidence that it is derived from the leucocytes. It is destroyed by exposure to room temperature for a few hours or to a temperature of 56° C. for thirty minutes. It does not act directly on antigen but only after the antigen has been acted upon by its antibody (sensitized). During the process of antigen-antibody-complement union the complement is destroyed or at least rendered inactive. This is known as "fixation of complement." In experimental work the fresh blood serum of a guinea pig is used as a source of complement because its complement content shows little variation in different animals and is comparatively high. Complement may be preserved by various chemical methods or by drying the fresh frozen guinea pig serum to a powder in a vacuum.

Antitoxins.—Antitoxins are antibodies that neutralize toxins. On account of their importance they will be accorded special consideration in the next chapter.

Bacteriolysins.—Antibodies that aid in the solution of cells are known as *cytolysins*. *Bacteriolysins* are cytolysins that cause the solution or lysis of bacteria. Cytolysis is dependent on the presence of both cytolytic antibodies and complement; if only one is present, cytolysis will not occur. The antibodies that take part in bacteriolysis are produced or at least increased by infection. A cytolysin of great importance in immunological procedures is known as *hemolysin* which causes hemolysis (the dissolution of red blood cells). It is prepared by giving an animal (most often a rabbit) a series of injections of the washed red blood cells of an animal of another species (most often man or sheep). Hemolysins develop in the blood serum of the animal receiving the injections. They affect the red blood cells of the species whose cells were injected but not those of other species. Cytolysins are often called *amboceptors*.

Agglutinins.—If the blood serum of a person who has had one of certain diseases is mixed with a suspension of the bacteria that cause that disease, the latter will adhere to each other and, in test tube experiments, form easily visible clumps that sink to the bottom of the tube. Likewise, if an experi-

mental animal receives several injections of certain bacteria, the blood serum of that animal will acquire the ability to cause the clumping of bacteria belonging to the species with which the animal was injected. This process is called *agglutination*. The antibodies that bring about agglutination are called *agglutinins*. Substances which upon injection into an animal bring about the formation of agglutinins are known as *agglutinogens*. Normal agglutinins may exist in the blood of certain persons. For instance, the blood serum of some people may show a weak agglutinin content for colon bacilli and typhoid bacilli although they have never been infected with these organisms. The agglutinin content is so low, however that when the serum is diluted 20 or 40 times and mixed with a suspension of one of these organisms, agglutination does not occur. *Immune agglutinins* are agglutinins brought about by infection or artificial immunization. Such agglutinins occur plentifully in the blood serum. For instance, such sera will often cause agglutination when diluted 500 or 1,000 times. Agglutinin formation is usually specific; i.e., when an organism is naturally or artificially introduced into the body it forms agglutinins against only itself or in some cases very closely related organisms. Agglutinins for the closely related organisms are known as *group agglutinins*. In all cases the agglutinin content of the serum is much higher for the organism bringing about the production of the agglutinins than it is for the closely related organism.

Infection or artificial immunization with comparatively few organisms leads to appreciable agglutinin formation. Most important of these are the members of the typhoid-colon group, *Br. abortus*, *Br. melitensis*, and *Past. tularensis*. In infections with these organisms the agglutination test becomes an important diagnostic procedure. For instance, if some of the blood serum of a patient suspected of having typhoid fever is mixed with a suspension of typhoid bacilli and agglutination is found to occur when the serum is diluted enough to exclude the action of natural and group agglutinins, we know that the patient's serum contains immune agglutinins against typhoid bacilli. We do not know

for certain, however, that the agglutinins are due to the present illness, because they might be due to a previous attack of typhoid fever or the recent taking of antityphoid vaccine. These questions are usually cleared by the case history and the clinical manifestations of the disease. This is the basis of the Widal test for typhoid fever. Other diseases in which the agglutination test is of diagnostic value are infections with other members of the typhoid-colon group of organisms, undulant fever, and tularemia. In the lower animals the agglutination test is used to detect Bang's disease (contagious abortion of cattle) and pullorum infections (bacillary white dysentery in chickens caused by *Salmonella pullorum*). It should be remembered that the body does not manufacture enough agglutinins to give a positive test until the infection has lasted a week or ten days.

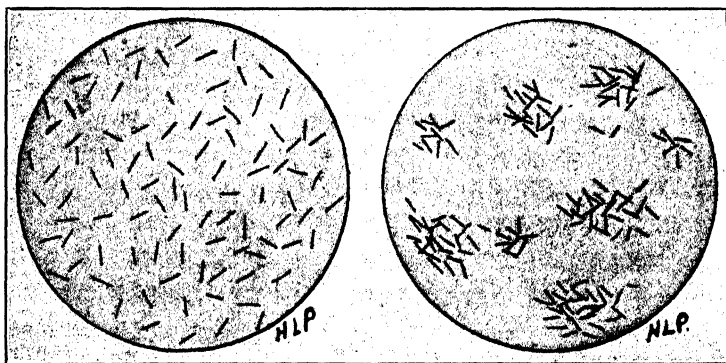


Fig. 61.

Fig. 62.

Fig. 61.—Microscopic appearance of negative agglutination test. Note the bacteria evenly spread through the preparation and the absence of clumping.

Fig. 62.—Microscopic appearance of a positive agglutination test. Note clumping of bacteria.

It has been found that in a few diseases agglutinins are produced against organisms which apparently have no relation to the disease. Such agglutinins are known as *nonspecific* agglutinins. The nonspecific agglutination test is of special diagnostic value in typhus fever. In this disease agglutinins develop against *B. proteus* an organism which

apparently has no relation to the disease. It is now thought that many nonspecific agglutinins are formed as the result of the introduction into the body of heterophile antigens (see page 198).

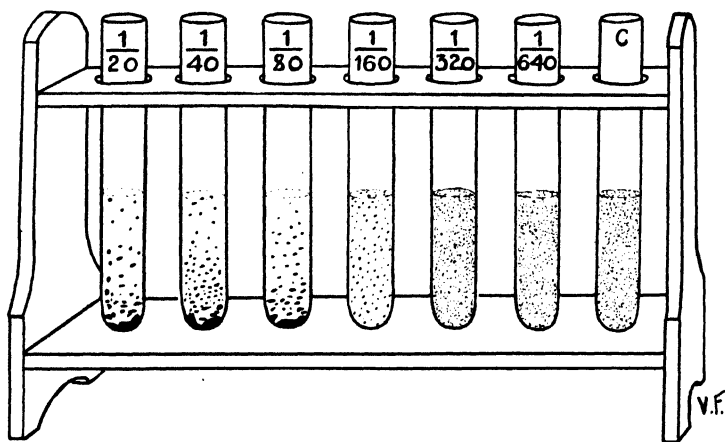


Fig. 63.—A test tube agglutination test (positive). Each tube contains 1 c.c. of the patient's diluted blood serum and an equal amount of a suspension of bacteria in salt solution. The bacteria have formed large clumps which have settled to the bottom in the first three tubes. Some clumping is seen in the fourth tube. None is present in the fifth and sixth tubes or in the seventh which acts as a control and contains salt solution instead of blood serum. The figures on the tubes indicate the dilution of the blood serum.

The agglutination test may be utilized for the identification of bacteria. In this case agglutinating serums are prepared by artificially immunizing animals with different known species of bacteria and mixing a suspension of the unknown bacteria with these serums. If one of the serums shows agglutination we know that the unknown bacteria are of the same kind as those against which the serum was prepared. After an animal has been immunized to produce an agglutinating serum the animal is bled, and the blood serum is separated from the cells and preserved for use. Such serums retain their potency for months. In the application of the agglutination test to the identification of bacteria the antibody is known and the antigen is unknown; in its application to the diagnosis of disease the antigen is known and the antibody is unknown.

The agglutinins discussed in the preceding paragraphs are by no means all the known agglutinins. For instance, the blood of each person falls into one of four groups, depending on the ability of its serum to agglutinate the cells of persons whose blood is in another group. This is due to the distribution of two agglutinins in the serum and two agglutinogens in the red blood cells. The agglutinins are known as *a* and *b*. The agglutinogens are designated *A* and *B*. Agglutinin *a* causes cells containing agglutininogen *A* to agglutinate. Agglutinin *b* causes cells containing agglutininogen *B* to agglutinate. The blood groups and their agglutinin and agglutinogen content are as follows:

Group AB: Serum contains no agglutinin; cells contain agglutinogens *A* and *B*.

Group A: Serum contains agglutinin *b*; cells contain agglutinogen *A*.

Group B: Serum contains agglutinin *a*; cells contain agglutinogen *B*.

Group O: Serum contains agglutinins *a* and *b*; cells contain no agglutinogen.

Precipitins.—When a suitable animal is immunized with certain bacteria, the animal's serum acquires the ability to cause precipitation of a clear filtrate of the bacteria. The same is true when an animal is immunized with the blood serum or other proteins of animals of different species or with certain vegetable proteins. Precipitins do not form in ordinary infections. Precipitins are specific; i.e., bacterial precipitins react only with filtrates of the bacteria that led to their production and precipitins formed by immunizing an animal with the blood serum of an animal of a different species react only with the proteins of the species used for immunization. The precipitin reaction has a wide medico-legal application in determining whether bloodstains are of human origin or otherwise.

Heterophile Antibodies.—Heterophile antibodies are those produced by an antigen which, upon gaining entrance to the animal body, produces antibodies not only against itself but against other antigens as well. Such antigens are known as

heterophile antigens and are common in the lower orders of life. It seems reasonable to assume that the formation of nonspecific agglutinins is, at least sometimes, due to the formation of heterophile antibodies. For instance, in the case of typhus fever the causative agent of the disease seems to be a heterophile antigen which brings about the formation of antibodies, not only against itself, but against *Proteus bacilli* as well. This explains why the blood serum of patients with typhus fever agglutinates *Proteus bacilli*. Another heterophile reaction which is put to diagnostic use is the development of agglutinins against the red blood cells of sheep in the blood serum of a person with infectious mononucleosis.



Fig. 64.—Technician reading agglutination tests. Note the masses of agglutinated bacteria which have sunk to the bottoms of the tubes.

Opsonins.—Opsonins are substances which act on bacteria or other cells in such a manner as to render them more easily ingested by phagocytes. They will be further discussed in connection with phagocytosis.

Virus-Neutralizing Antibodies.—Some virus diseases (e.g., measles and smallpox) are followed by a lasting immunity; others (e.g., common colds and influenza) are followed by an immunity of short duration. The antibodies which bring about an immunity to viruses are known as *virus-neutralizing antibodies*. The exact nature of virus-neutralizing antibodies is not known, but it is reasonable to believe that they do not differ greatly from antibodies in general.

II. Phagocytosis

The ingestion of bacteria or other particulate matter by the body cells is known as *phagocytosis* and the body cells that are capable of ingesting such materials are known as *phagocytes*. Phagocytosis bears a close resemblance to the feeding process of unicellular organisms and is a universal response on the part of the body to invasion by bacteria, alien cells, or other foreign particles. It is an essential feature in protecting the body against infection and probably plays an important part in natural immunity. Phagocytosis is a general process because although only a few kinds of body cells have the power of phagocytosis, they are capable of ingesting many different kinds of particulate matter, such as bacteria, dead body cells, mineral particles, dust, and pigment and in some cases substances in solution.

The important phagocytic cells are the leucocytes, especially the polymorphonuclear variety and certain cells of the reticuloendothelial system. While the phagocytes attempt to destroy bacteria after ingesting them, they may fail to do so, and the phagocytes themselves may be destroyed with liberation of the ingested bacteria. Relatively harmless organisms are usually completely destroyed after ingestion. In some cases the bacteria continue to multiply in the cytoplasm of the cell. The student who wishes to see bacteria undergoing phagocytosis should stain a smear from an ordinary boil where staphylococci will be found within the cytoplasm of the leucocytes. Smears from gonorrheal exudates and from the cerebrospinal fluid in epidemic meningitis usually show organisms in the cyto-

plasm of the leucocytes, i.e., undergoing phagocytosis. Purulent exudates consist chiefly of phagocytic cells that have been attracted to the site of infection. Different bacteria show difference in their resistance to phagocytosis. For instance, gonococci undergo phagocytosis easily, while *Myco. tuberculosis* and *B. anthracis* are quite resistant to phagocytosis. The degree of phagocytosis occurring when the white blood cells of a person or animal suspected of having a disease are mixed with a suspension of the bacteria causing the disease, is of diagnostic significance. Such tests are known as *opsonocytophagic* tests. They are of special value in the diagnosis of undulant fever and tularemia.



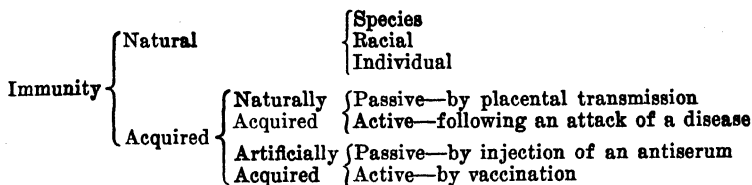
Fig. 65.—Phagocytosis by polymorphonuclear leucocytes. Diplococci are found in the cytoplasm of seven of the cells. The larger dark structures are the nuclei of the leucocytes.

Phagocytosis is not an activity of the phagocytes alone but is dependent on the action of substances in the serum, known as *opsonins*, that act on the bacteria and render them more susceptible to the action of phagocytes. Opsonins are to some degree present in normal serum but are present in an increased amount in immune serum. The action of opsonins is enhanced by the presence of complement. The

relation of opsonins to phagocytosis is strong proof of the interrelation of humoral and cellular elements in the process of immunity.

III. Kinds of Immunity

Immunity may be classified in a number of ways. One example is given below:



In the preceding classification immunity is primarily classified as natural and acquired.

A *natural* immunity is a more or less permanent one with which a person or lower animal is born; i.e., it is a natural heritage. It may be the heritage of a species, race, or individual. *Species* immunity is that immunity peculiar to a species. For instance, man does not have many of the diseases of the lower animals and vice versa. A *racial* immunity is one possessed by a race. For instance, ordinary sheep are very susceptible to anthrax, while Algerian sheep seldom contract the disease. Natural individual immunity is a rare condition and most so-called cases can be explained by unrecognized infections. Natural immunity can best be explained by the action of phagocytes and the natural bactericidal power of the blood.

An *acquired* immunity is one resulting from the transmission of antibodies by way of the placenta, an attack of a disease, vaccination or the administration of an antiserum against a disease. It is never the heritage of a species, race, or individual. It may be naturally acquired by the transmission of antibodies from the mother to the fetus by way of the placenta or by having an attack of a disease. It may be artificially acquired by vaccination or the administration of an immune serum.

Depending on the part played by the body cells of the animal or person being immunized, immunity may be clas-

sified as *active* and *passive*. If a person has an attack of typhoid fever or smallpox or is vaccinated against these diseases his body cells respond to the presence of the antigen by producing antibodies that destroy the causative agent of the disease should it ever gain access to the body again. This is an *active* immunity because it was brought about by the activity of the body cells of the person that became immunized. All naturally acquired immunities except those transferred to the child from the mother by way of the placenta are active immunities. Examples of active immunities artificially acquired are those following vaccination against typhoid fever or smallpox, the Pasteur treatment, and the administration of toxin-antitoxin or toxoid to prevent diphtheria.

When the serum of an actively immunized animal is injected into the body of a nonimmune animal (example—the injection into a child of diphtheria antitoxin which is the refined and concentrated blood serum of a horse that has been actively immunized against diphtheria toxin) the latter becomes temporarily immune. This is called *passive* immunity because the immunity-producing principle was introduced in the injected serum, and the cells of the animal becoming immunized took no part in the process, i.e., they were passive. Young infants may show a passive immunity to such diseases as measles, smallpox, diphtheria, etc., due to a transfer of immune bodies from the blood of the mother to the child via the placenta. Naturally, the child will not inherit such an immunity if the mother is not immune. With this exception all passive immunities are established by the administration of an immune serum (the serum of an animal that contains antibodies because the animal has been actively immunized: example—diphtheria antitoxin, tetanus antitoxin, antimeningococcus serum). The production of passive immunity shows its most brilliant application in the use of diphtheria antitoxin to prevent and cure diphtheria and of tetanus antitoxin to prevent tetanus.

In the interest of sound therapeutic principles it should be borne in mind that an active immunity can be established only by having a disease or being vaccinated (see definition

of vaccine, page 212) against it, and that the immunity is slowly established and of long duration (months or years), while a passive immunity is ordinarily established at once by the injection of an immune serum and is of short duration (one or two weeks). Upon these facts is based the principle of producing an active immunity when there is no immediate danger of a disease and establishing a passive immunity when there is immediate danger of a disease or the patient is already ill.

IV. The Relation Existing Between Exposure to Disease and Immunity

It seems that when an infectious disease attacks a population that has never been exposed to that disease, the number of people attacked is very high and many of those attacked succumb to its ravages. On the other hand, when an epidemic of a disease that has been endemic in a population for years occurs, the number of people attacked and the percentage of deaths among those attacked decreases. There is little doubt that syphilis was at one time a far more virulent and fatal disease than it now is. The susceptibility of aboriginal people to tuberculosis is much greater than that of the people of communities in which the disease has existed for a long time. When measles was first introduced into the Fiji Islands in 1875 almost 30 per cent of the population died. Scarlet fever has become milder in Western Europe and America since 1880. The lessened susceptibility of the population to a disease that has existed in a country for a long time is due to the fact that through exposure for generation after generation people develop a more or less general immunity to that disease. What exposure to infectious agents through even a few years will do was well illustrated during World War I. When recruits were brought into training camps, sickness and death was much more common among the country recruits who had seldom before been exposed to infection than among the city recruits who were brought up under conditions of more or less constant exposure. It has been said that the white man subjugated the American Indian more by the diseases he brought to him, to which the Indian possessed no

immunity, than he did by superior knowledge or more effective weapons. In this conquest by disease the white man had a mighty ally—the Negro slave.

V. Immunological Methods of Studying Bacteria and Diagnosing Disease

Among the immunological methods of studying bacteria and diagnosing disease, the following may be mentioned:

1. The complement fixation test for syphilis and certain other diseases.
2. Precipitation tests for syphilis.
3. Agglutination tests for such diseases as typhoid fever, paratyphoid fever, undulant fever, tularemia, typhus fever, and Rocky Mountain spotted fever.
4. The Schick test for susceptibility to diphtheria and the Dick test for susceptibility to scarlet fever.
5. The tuberculin test and the intradermal test for undulant fever.
6. The Frei test.
7. The protein precipitation tests which are of value in determining the origin of proteins. A practical application is the determination of the human or lower animal origin of blood stains as used in the detection of crime.
8. The identification of unknown bacteria by agglutinating them with known antisera.
9. The typing of pneumococci and meningococci.
10. The determination of the strength of various antitoxins and antisera.

VI. The Principle of Complement Fixation

This topic is discussed here because upon it depends the highly important Wassermann test for syphilis as well as the complement fixation test for other diseases. The test has for its purpose the detection of antibodies against a certain disease and is based on this fact: when blood serum containing antibodies against a disease, the causative agent of that disease, and complement (see page 193) are mixed in suitable proportions and incubated, the three enter into some kind of combination whereby the complement is destroyed or otherwise rendered inactive. This is spoken of

PLATE I

FIG. 1.—Reading of Results of Wassermann Test. The first tube shows complete inhibition of hemolysis and may be read four-plus.

Tubes 2 and 3 show three-plus and two-plus reactions.

Tubes 4 and 5 show single-plus and plus-minus reactions.

Tube 6 shows a negative reaction.

FIG. 2.—Wassermann Test. Positive Reaction. Tube 1 contains the patient's blood serum and syphilitic antigen and shows complete inhibition of hemolysis or a positive reaction. Tube 2 is a control of the patient's serum without antigen, and shows complete hemolysis. Tube 3 is a known syphilitic control serum. Tube 4 is a control of the positive serum, without antigen. Tube 5 is a known normal serum and Tube 6 a control of the normal serum without antigen.

FIG. 3.—Wassermann Test. Negative Reaction. Tube 1 contains the patient's blood serum and syphilitic antigen and shows complete hemolysis, or a negative reaction. Tube 2 is a control of this serum without antigen. Tube 3 is a known positive serum and shows complete inhibition of hemolysis. Tube 4 is a control of the known positive serum without antigen. Tube 5 is a known normal serum with the antigen and Tube 6 a control of the normal serum without antigen.

NOTE: In Fig. 1 the top row of + 's indicates the usual method of reading the reaction. The bottom row indicates the special method of Dr. Craig.

(From Craig: *The Wassermann Test*, The C. V. Mosby Co.)

as "complement fixation." Let us see how this phenomenon is applied to the diagnosis of disease. If the blood serum of a person who has had a gonorrheal infection of sufficient extent to bring about antibody production is mixed with suitable amounts of complement (the fresh blood serum of a guinea pig) and a suspension of gonococci, the three will

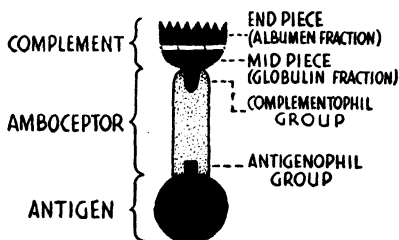


Fig. 66.—Illustration of the manner in which complement combines with antigen. Amboceptor is known also as sensitizer. (From Rice: *A Textbook of Bacteriology*. W. B. Saunders Co.)



Fig. 67.—Technician setting up complement fixation tests for syphilis. At the left are two racks showing the titration of hemolysin and complement. The rack at which the technician is working is the main test. This rack contains 25 tests.

enter into a combination whereby the complement is rendered inactive, i.e., "fixed." This combination is not accompanied by any visible change, and to detect such a combination we must add some kind of indicator. We have such an indicator in hemolysin or amboceptor which brings about a combination between complement and the cells of the species of animal against which it was prepared that causes

hemolysis of the cells. Hemolysis is an easily visible phenomenon. If to the mixture of patient's blood serum (containing antibodies), complement, and gonococcus suspension (the antigen) suitable proportions of hemolysin and red blood cells are added and the mixture is incubated a second time, hemolysis will not occur because the complement has been fixed by the antigen-antibody-complement combination of the first incubation. This is a positive test and is graphically illustrated as follows:

First Incubation:

Patient's serum (antibodies)	}	=	{	Antigen-antibody-complement combination (Complement rendered in active or "fixed").
+				
Complement				
+				
Gonococci (antigen)				

Second Incubation:

Antigen-antibody complement combination (formed during the first incubation)	}	=	{	No hemolysis because complement has been rendered inactive ("fixed").
+				
Hemolysin				
+				
Red blood cells				

If, on the other hand, the patient's serum does not contain antibodies, the complement will not be fixed during the first incubation and hemolysis will occur when hemolysin and red blood cells are added. This is a negative test and is graphically illustrated as follows:

First Incubation:

Patient's serum (no antibodies present)	}	=	No change; complement not fixed.
+			
Complement			
+			
Gonococci (antigen)			

Second Incubation:

Patient's serum (No antibodies)	}	{	=	{	Complement which has not been affected during first incubation combines with hemolysin and red blood cells to produce hemolysis.
+					
Complement					
+					
Gonococci	}	}	}	}	
+					
Hemolysin					
+					
Red blood cells					

Since it is almost impossible to grow the causative organisms of syphilis by artificial methods, extracts of the livers of syphilitic fetuses were used as antigens when the Wassermann test first came into use. These extracts were used because the liver of a syphilitic fetus contains myriads of the causative organisms of syphilis, and such extracts were the nearest approach to extracts of the organisms themselves. Since that time it has been found that certain lipoidal extracts of normal organs are more efficient antigens than extracts of syphilitic livers. Of course the term "antigen" as applied to such extracts of normal tissue in connection with the Wassermann test is scientifically incorrect. The antigens used in complement fixation tests for gonorrhea and tuberculosis are extracts of gonococci and tubercle bacilli, respectively.

Questions for Review

1. Fill out the following table, indicating whether each example is (1) a natural or acquired immunity, (2) if acquired, whether natural or artificially acquired, and (3) whether an active or passive immunity.

CAUSE OF IMMUNITY	NATURAL	ACQUIRED	IF ACQUIRED		ACTIVE	PASSIVE
			NATURALLY	ARTIFICIALLY		
An attack of typhoid fever						
An attack of smallpox						
Vaccination against typhoid fever						
Vaccination against smallpox						
The Pasteur treatment						
Diphtheria antitoxin						
Diphtheria toxin-antitoxin						
Tetanus antitoxin						
Diphtheria toxoid						
Antimeningococcus serum						
Bacterial vaccine						
Immunity transmitted from mother to newborn child						

2. List the various immunological methods of studying bacteria.
3. Discuss the principles of complement fixation. In what diagnostic tests is complement fixation the basis?
4. What is the lessened susceptibility of a population to a disease that has existed in a given area for a long time due to?

True-False Test

Place the word "true" or "false" before each statement.

- 1. Immunity, in a narrow sense, is the resistance possessed by an animal to infection.
- 2. Scarlet fever confers a slight degree of immunity of short duration.
- 3. Today the two theories of immunity are not considered as opposing theories.
- 4. Antigens are of protein nature.
- 5. The antigen-antibody reaction is not always specific.
- 6. Many immunologists believe that the antibodies are a special type of globulin produced by the cells.
- 7. Antibodies have been isolated from the blood.
- 8. *Ehrlich's side-chain theory of antibody production* has been scientifically proved.
- 9. In *Ehrlich's side-chain theory of antibody production*, the cast-off receptors are known as the "antibodies."
- 10. Complement is a component of fresh blood serum and is not increased by immunization.
- 11. Bacteriolysins are antibodies that cause organisms evenly suspended in a liquid to adhere to each other and form clumps.
- 12. Agglutinins are antibodies that aid in the solution of cells.
- 13. In order for agglutination to occur, both the agglutinin and agglutigen must be present.
- 14. Heterophile antibodies are those produced by an antigen which, upon gaining entrance to the body, produces antibodies not only against itself, but also against other antigens as well.
- 15. Phagocytosis is considered an essential feature in protecting the body.

Completion Test

1. Susceptibility signifies the ----- of immunity.
2. Ehrlich established the ----- or ----- theory of immunity.
3. Metchnikoff, French immunologist, established the ----- or ----- theory of immunity.
4. A substance giving rise to the formation of antibodies is known as an -----.

5. According to action, antibodies may be classified as follows:
 -----,
 -----, and -----.
6. During the process of antigen-antibody-complement union the complement is rendered inactive and this is known as "-----."
7. The agglutination test for diagnosing typhoid fever is known as the ----- test.
8. Define hemolysis.
9. The precipitin reaction is of importance in diagnosing the types of -----.
10. The ingestion of bacteria or other particulate matter by the body cells is known as -----.
11. The most important phagocytic cells are the -----, especially the ----- variety.
12. Phagocytosis is not an activity of the phagocytes alone but is dependent also on the action of substances in the serum known as -----.

References

- Topley and Wilson: Principles of Bacteriology and Immunology, Baltimore, 1946, Williams & Wilkins Co.
- Sherwood, N. P.: Immunology, St. Louis, 1941, The C. V. Mosby Co.
- Zinsser and Bayne-Jones: Textbook of Bacteriology, New York, 1939, D. Appleton-Century Co.
- Jordan, Edwin O., and Burrows, William: Textbook of Bacteriology, Philadelphia, 1945, W. B. Saunders Co.

CHAPTER XVII

VACCINES AND IMMUNE SERUMS

There is a tendency on the part of physicians and nurses to confuse the terms "vaccine" and "immune serum," any product of this nature being spoken of as a "serum." Vaccines and immune serums differ in their fundamental basis, method of production, and type of immunity that they bring about.

A *vaccine* is the causative agent of a disease (bacterium, toxin, or virus) modified in such a manner that it is incapable of producing the disease but at the same time it is so little changed that it is able when introduced into the body to elicit the production of specific antibodies against the disease. Vaccines are always antigens; i.e., they always produce an active immunity. They find their greatest usefulness in the prevention of disease. Important vaccines are those for the prevention of typhoid fever, small-pox and rabies; toxin-antitoxin and toxoid to prevent diphtheria, toxin to prevent scarlet fever, tetanus toxoid for bringing about a more or less permanent immunity to tetanus and the more recently introduced staphylococcus toxoid. All of these except scarlet fever toxin are the causative agents of their respective diseases, so modified that they are no longer capable of causing the disease but are still capable of bringing about the production of immune bodies against it. Instead of modifying scarlet fever toxin itself, the dose is modified; i.e., it is given in a series of doses so small that they are not injurious.

An *immune serum* is the serum of an animal that has been highly immunized to an infectious disease. Its characteristic feature is the antibodies that it contains. Immune serums bring about only passive immunity; i.e., the immunity that they confer is due to the antibodies they contain. Both vaccines and immune serums are specific in their action; i.e., they bring about an immunity to no disease other

than the one for which they were prepared. Immune serums are of two types: antitoxic and antibacterial.

Antitoxins.—Antitoxins are immune serums that neutralize toxins. They may be artificially prepared and they develop in the body as a result of repeated slight infections. The latter is the reason why most adults are immune to diphtheria. Antitoxins have no action on the bacteria that produce the toxins. For example, diphtheria antitoxin neutralizes diphtheria toxin in the tissues and circulation but has no effect on the diphtheria bacilli that are growing in the throat and producing the toxin. Why the membrane in the throat disappears after the administration of antitoxin will be discussed later.

Antitoxins can be successfully prepared only against exotoxins. The antitoxins that have been used longest and have saved most lives are those against diphtheria and tetanus. Both are prepared in the same general way. The bacteria are allowed to grow in a liquid medium until the medium contains a large amount of exotoxin that has been thrown off by the bacteria. In some cases one cubic centimeter of a broth culture of tetanus bacilli may contain enough toxin to kill 75,000 guinea pigs. After the bacilli have grown long enough, they are separated from the medium, and the toxin content of the medium is determined. It is necessary to determine the strength of each lot of toxin or antitoxin because two lots prepared exactly alike seldom have the same strength. The unit of toxin measurement is known as the *minimum lethal dose* (M. L. D.). It is the amount of toxin which when injected into a test animal will kill it in a definite time. For diphtheria toxin it is the amount that will kill a guinea pig weighing 250 grams in four days, and for tetanus toxin it is the amount that will kill a 350 gram guinea pig in the same length of time. When the toxin is found to be of suitable strength, horses are immunized against it by beginning with a small dose and giving several injections, increasing the dose at each injection. In immunizing horses for the production of diphtheria antitoxin, toxoid may be used instead of toxin. At the time which

experience has shown antitoxin production to be at its height, the horse is bled and the antitoxin strength of his blood serum is tested. If the blood serum is found to contain sufficient antitoxin, it is further refined and purified for use. Without going into the details of standardization, we will say that a *unit* of diphtheria antitoxin is considerably more than enough to neutralize 100 M. L. D. of diphtheria toxin and that a unit of tetanus antitoxin is an amount sufficient to neutralize 1,000 M. L. D. of tetanus toxin.

Since antitoxin can be successfully prepared only against organisms producing extracellular toxins and since few organisms produce extracellular toxins, the number of antitoxins is limited. An antitoxin against the toxin of the scarlet fever streptococcus is being used with considerable success. The unit of measurement of scarlet fever streptococcus toxin is known as the "skin test dose" (S. T. D.) which is the smallest amount that will cause a reaction when injected intradermally into a susceptible person. A unit of scarlet fever antitoxin is the amount that will neutralize 50 S. T. D. of scarlet fever streptococcus toxin. Botulinus antitoxin has been used with good results. Reports seem to indicate that erysipelas streptococcus antitoxin and staphylococcus antitoxin are of benefit. All antitoxins should be given early and in sufficient amount because they cannot repair injury already done.

Antivenins.—Antivenins have been prepared against the venoms of snakes and the black widow spider. They are prepared in the same general way as other antitoxins; that is, by immunizing a horse with repeated doses of snake venom or the venom of the black widow spider. Antivenins may be prepared against a single species of snakes or groups of closely related species. Whether snake antivenin is prepared against a species or a group of closely related species depends on the geographical location where it is to be used. North American antislake bite serum (also known as antivenin and *Crotalus* antitoxin) is effective against rattlesnakes, copperheads, and cotton mouth moccasins. These are the most common poisonous snakes of North America. It is not effective against the venom of the coral snake. The use

of antivenin in snake bite and the bite of the black widow spider should in no way replace first-aid and supportive measures.

Antibacterial Serums.—These serums owe their action to their ability to destroy bacteria. At the present it is thought that they act by combining with some antigen on the surface of bacteria and rendering them more susceptible to the action of leucocytes. Such serums are those against meningococci (antimeningococcus serum), pneumococci (antipneumococcus serum), staphylococci, and dysentery bacilli (antidysenteric serum). Antidysenteric serums may be either antitoxic or antibacterial, depending on the type of *B. dysenteriae* against which they are prepared. Depending on their method of manufacture and the strains of staphylococci used, antistaphylococcal serums may be either antibacterial or antitoxic. Antibacterial serums are prepared by injecting horses with the bacteria in question. The employment of rabbits for the production of antipneumococcus serum is of recent development. This serum seems to have several advantages over antipneumococcus serum produced from the horse. A *polyvalent* antibacterial serum is one prepared against several strains of bacteria. A *univalent* serum is one against a single strain. For instance, antipneumococcus serum was formerly polyvalent because we did not know of the thirty-two types of pneumococci and the horse was immunized with a mixture of pneumococci obtained from several different sources; therefore, by the law of chance several strains would be represented. At the present time antipneumococcus serum is univalent; that is, each type of pneumococcus has its own specific type of antiserum.

Convalescent Serum Therapy.—Convalescent serum therapy consists of injecting the whole blood or serum of a person who has recently recovered from a disease into one ill of the disease (as a therapeutic measure) or one exposed to the disease (as a preventive measure). The theory on which this type of therapy is based is that the blood of the convalescent patient contains antibodies, and these antibodies confer a passive immunity upon a person to whom the blood is given. This type of therapy has been used with

good results in measles, poliomyelitis, and scarlet fever. The author believes that he has seen its beneficial effects in mumps. Human placental extract has been used to prevent or modify the attack of measles. Its results are encouraging. Caution should be observed in giving convalescent serum because it may transmit the agent of homologous serum jaundice.

How Vaccines Are Prepared.—Bacterial vaccines are suspensions of killed bacteria in salt solution. A culture of the bacteria is grown for a short time (twenty-four to forty-eight hours). If grown on slants the bacteria are washed off by means of a swab and sterile salt solution. The number of bacteria in each cubic centimeter of the washings is determined and salt solution is added until the desired number per cubic centimeter is obtained. The bacteria are then killed at the lowest possible temperature in the shortest possible time. In some cases they are killed by adding formalin or tricresol to the vaccine without heating. Cultures are made from the finished product to see that the bacteria are dead. The number of bacteria given at a single injection ranges from 100,000,000 to 1,000,000,000. Bacterial vaccines are of two types: *stock vaccines* made from stock cultures maintained in the laboratory and *autogenous vaccines* made from cultures obtained from the lesions for which the vaccine is being made. A *mixed vaccine* is one containing bacteria belonging to two or more species; for instance, one containing staphylococci and streptococci. A *polyvalent vaccine* is one containing several strains of organisms belonging to the same species; for instance, one containing several strains of staphylococci or streptococci. By strains of bacteria are meant groups of bacteria within a species characterized by some particular quality; for instance, there are many strains of streptococci (that is, within the species there are many groups of closely related bacteria).

Bacterial vaccines have been recommended for many diseases, but they show their best results in localized infections, particularly boils, and as a preventive of typhoid fever. The theory of their action is that they increase phagocytosis and cause tissues not involved in the disease

process to produce antibodies. Although we would not expect such to be the case, bacterial vaccines seem to be of value in certain acute infections.

Smallpox vaccine is prepared by the inoculation of female calves from six months to one year old with cowpox virus. The abdomen is shaved and rendered sterile. It is then scratched with a needle (scarified) in many places. The scratches should be just deep enough to bring a little blood. The virus is rubbed into these scratches. At the end of about six days the abdomen will be thickly broken out with vesicles which contain the modified virus used for vaccination. With the most perfect aseptic technic, the tops of the vesicles are opened, and the sticky exudate is removed. The exudate is then mixed with four times its weight of equal parts of glycerin and water containing 1 per cent phenol for preservation. The vaccine is now purified, and, if found to be of sufficient potency and sterile, is ready for use. Some manufacturers add brilliant green to the vaccine for the purpose of inhibiting bacterial growth. They also paint the vaccinated area on the calf with this dye. Recently there has been considerable experimental work on the production of smallpox vaccine by growing it artificially in the presence of the bacteria-free tissues of the chick embryo. If smallpox vaccine is not shipped and stored at near-freezing temperature, it rapidly loses its potency.

Rabies vaccine is prepared from the brain and spinal cord of rabbits suffering with rabies. The rabbit is inoculated with rabies, and just before death the brain and cord are removed under the strictest aseptic precautions. The cord, or brain and cord are now subjected to procedures which render them incapable of producing rabies but which do not interfere with their stimulation of the production of antibodies against the disease. This may be accomplished by drying, dilution, freezing, or chemical treatment. The vaccine is given as an emulsion prepared by grinding the material with water or salt solution either during the process of attenuation or after it is complete. A treatment consists of 14 to 28 doses. In rabies vaccine we have

an exception to the rule that on account of the time required to establish it, the production of an active immunity cannot be depended upon to protect those already exposed to a disease. This is because the incubation period of rabies is much longer than that of most diseases, and an active immunity can be established before the time for the disease to begin. It is fortunate that this is the case because there is no known method of establishing a passive immunity.

Toxin-antitoxin is a mixture of diphtheria toxin and antitoxin with a slight excess of the former. It is used for producing a permanent immunity to diphtheria but cannot be used to prevent the disease in those already exposed. A treatment consists of three injections given at weekly intervals. It takes three months or more for the immunity to become completely established.

Diphtheria toxoid is diphtheria toxin which has been incubated with formaldehyde. This reduces its toxicity but preserves its antigenic properties; i.e., it is not capable of causing diphtheria but is capable of stimulating the body cells to produce diphtheria antitoxin. Its use is the same as that of toxin-antitoxin. If alum is added to diphtheria toxoid the antigenic portion of the toxoid is precipitated. The precipitate, after being washed and suspended in sterile salt solution, is known as *diphtheria toxoid, alum precipitated*. Its advantage is that when injected into the body, it is absorbed slowly, which gives a prolonged antigenic stimulation. Two doses at three- or four-week intervals usually produce an immunity.

Tetanus toxoid, which is prepared along the same general lines as diphtheria toxoid, is used to establish a permanent immunity to tetanus. It is routinely used in the U. S. Army. It is manufactured in the ordinary and alum-precipitated forms.

Most manufacturers are now marketing a mixture of diphtheria and tetanus toxoids. This combination is meeting with considerable favor.

Staphylococcus toxoid prepared from the toxin of staphylococci is of value in certain acute and chronic staphylococcus

infections. It may be prepared in the ordinary or alum-precipitated forms.

Scarlet fever streptococcus toxin is given subcutaneously in small but increasing doses until from three to five injections are given for the purpose of bringing about a more or less permanent immunity to scarlet fever.

Yellow fever vaccine gave excellent results as a preventive of yellow fever in the Allied armies during World War II. It is prepared by growing an attenuated yellow fever virus in chicken embryos. The vaccine acts by giving the person a subclinical or mild attack of yellow fever. It is prepared in the following manner: Fresh fertile eggs are incubated as for hatching for seven or eight days. A small hole is bored in the center of the broad end of each egg and a little virus is introduced into the neighborhood of the developing embryo. The eggs are then allowed to incubate 90 to 96 hours longer, after which they are broken and the developing embryos are removed and rubbed into a homogeneous mass. A small amount of salt solution is added and the material is centrifuged. The supernatant fluid is placed in a temperature of below freezing and dried to a powder. This powder is preserved at a below-freezing temperature and diluted with a salt solution just before using. In one method of manufacture blood serum is added to the vaccine as a preservative. The use of this vaccine has been followed by homologous serum jaundice which may give rise to serious manifestations.

Influenza virus vaccine is prepared in the same general way as yellow fever vaccine with these exceptions: after growing in egg the influenza virus is treated with formalin, and the methods of concentrating the virus differs from that of concentrating yellow fever virus.

Vaccines for the prevention of the *Rickettsial diseases* (typhus fever, Rocky Mountain spotted fever, etc.) are made in the same general way as yellow fever and influenza virus vaccines. A vaccine effective in preventing Rocky Mountain spotted fever has been prepared from grinding up infected ticks.

Manufacturing, Labeling, and Dating Serums, Vaccines. Etc.—It is so important that serums, vaccines, etc., be both of proper potency and free from bacterial contamination that, when offered for sale

in interstate commerce, they are manufactured under the license and regulations of the Federal Government. This supervision is delegated to the National Institute of Health.

Each package must show the name of the product, the name of the manufacturer, the license number of the manufacturer, the lot number, and the date of manufacture, issue or expiration. The date of issue is the date upon which the product is placed on the market. This must be within a certain time after manufacture, depending on the kind of product and the temperature of storage.

By the expiration date is meant the date beyond which the product cannot be expected to exert its full potency. For instance, if a package of diphtheria antitoxin has a stated potency of 10,000 units and an expiration date of Sept. 1, 1952, it means that properly stored the package will contain 10,000 units of diphtheria antitoxin on Sept. 1, 1952. This is provided for by putting an excess of antitoxin in the package. For an expiration date four years after date of manufacture an excess of 50 per cent is added; for three years, an excess of 40 per cent; for two years, an excess of 30 per cent; and for one year, an excess of 20 per cent. In other words, at the time of manufacture a 10,000 unit package of diphtheria antitoxin with a four-year dating contains 15,000 units of antitoxin, while one of the same size but a one-year dating contains only 12,000 units of antitoxin. Tetanus antitoxin is dated in the same manner as diphtheria antitoxin.

The expiration date of most other antitoxins is one year after manufacture or issue; for most antisera except antimeningococcus serum (six months), one year; for bacterial vaccines, eighteen months; for toxoids, two years; for smallpox vaccine and rabies vaccine, three months.

Questions for Review

1. How is smallpox vaccine prepared? From what is rabies vaccine prepared?
2. What is the unit of scarlet fever antitoxin? What is a "skin test dose"?
3. Discuss the preparation of diphtheria toxoid and diphtheria toxin-antitoxin.
4. State in a general way how yellow fever and influenza virus vaccines are prepared.

True-False Test

Place the word "true" or "false" before each statement.

- 1. Vaccines are always antigens and always produce an active immunity.
- 2. As a result of repeated infections, the body may develop antitoxins that neutralize toxins.
- 3. A unit of tetanus antitoxin is an amount sufficient to neutralize 100 minimal lethal doses of tetanus toxin.

- 4. Antitoxin can be successfully prepared only against organisms producing intracellular toxins.
- 5. Antivenins are prepared in the same general way as other antitoxins; that is, by immunizing a horse by repeated doses of snake venom.
- 6. A mixed vaccine is one containing bacteria belonging to two or more species.
- 7. At the present time antipneumococcus serum is univalent.

Completion Test

- 1. Some important vaccines are those for the prevention of -----, -----, and -----.
- 2. Immune serums contain ----- and bring about a ----- immunity.
- 3. Immune serums are of two types: ----- and -----.
- 4. Convalescent serum therapy confers a ----- immunity upon the person to whom the blood is given.
- 5. A vaccine made from cultures obtained from the lesions for which the vaccine is being made is called an -----.
- 6. Antibacterial serums owe their action to their ability to destroy -----.

References

- Sherwood, N. P.: Immunology, St. Louis, 1941, The C. V. Mosby Co.
- Gradwohl, R. B. H.: Clinical Laboratory Methods and Diagnosis, St. Louis, 1948, The C. V. Mosby Co.
- Jordan, Edwin O., and Burrows, William: Textbook of Bacteriology, Philadelphia, 1945, W. B. Saunders Co.
- American Medical Association: New and Nonofficial Remedies, 1946.
- Topley and Wilson: Principles of Bacteriology and Immunology, Baltimore, 1946, Williams & Wilkins Co.

CHAPTER XVIII

HYPERSENSITIVENESS

If a small amount of foreign protein (blood serum, egg white, etc.), which within itself is not poisonous, is injected into a suitable animal, this dose will be without noticeable effect; but if a second injection is given after an interval of from ten to fourteen days, severe symptoms or even death may occur. This condition is known as *anaphylaxis* (without protection in contradistinction to prophylaxis or protection). The first dose is known as the *sensitizing* dose; the second is known as the *provocative* dose. When the injections are given at closer intervals, for instance, every two or three days, immunity instead of anaphylaxis results.

Certain people exhibit unusual manifestations upon coming in contact with substances, usually of a protein nature, that have no effect on the average person. For instance, certain persons have asthma upon coming in contact with horse dander, feathers, etc. A great many have hay fever upon coming in contact with pollens, and others have skin eruptions or asthma after eating certain foods. Such diseases are known as *allergic diseases*, and the condition of increased susceptibility underlying their occurrence is known as *allergy* (altered reactivity). Substances that are capable of bringing about the allergic state are known as *allergens*.

As we shall attempt to show in subsequent paragraphs, anaphylaxis and allergy are fundamentally much alike, if not identical. For this reason the term *hypersensitiveness*, which includes both anaphylaxis and allergy, has come into general use. By hypersensitiveness is meant a condition in which the affected animal or person exhibits a marked reaction to substances that have little or no effect on a normal individual of the same species. With these explanations we may briefly summarize as follows: hypersensitiveness occurs in two forms—anaphylaxis and allergy. By anaphylaxis is meant the experimental hypersensitiveness produced in laboratory animals by introducing into their

bodies substances capable of bringing about the hypersensitive state. Allergy is a term applied to the natural or spontaneous form of hypersensitiveness of man which includes such conditions as hay fever, asthma, etc., and to such induced hypersensitive states as serum sickness, etc.

Anaphylaxis.—Before attempting a discussion of hypersensitiveness in general the salient features of anaphylaxis should be reviewed, because the experiments of anaphylaxis have answered many of the questions relating to hypersensitiveness in general. The phenomenon of anaphylaxis may be best demonstrated by giving a guinea pig a small injection of horse serum and at the end of ten to fourteen days giving a second but larger injection. Within one or two minutes the pig will become restless and exhibit difficulty in breathing which progresses to frantic activity with extreme dyspnea, followed by death from respiratory failure. At autopsy the lungs of the animal will show a remarkable resemblance to those of a person with asthma. If a rabbit is used as the test animal, death is due to circulatory failure and in the dog the symptoms are referable to the gastrointestinal tract. The symptoms of anaphylaxis depend on the species of the affected animal and not on the substance that brings about the anaphylactic state. Anaphylaxis is specific; i.e., for anaphylaxis to occur the sensitizing and provocative doses must be of the same substance. If the blood serum of a sensitized animal is injected into a normal animal and after an interval of from six to eight hours the normal animal is injected with some of the material to which the first animal is sensitive, anaphylactic symptoms will occur. This is known as *passive anaphylaxis*. The passive transfer of the hypersensitive state assumes considerable importance when it is realized that the use of a hypersensitive donor for blood transfusion may render the recipient hypersensitive. One interesting case of such a nature is reported in which after receiving blood from a donor that was sensitive to horse dander, the recipient had an attack of asthma each time he came near horses. If an animal survives an anaphylactic attack, it becomes desensitized for a time but eventually becomes sensitive again.

Theories of the Cause of Anaphylaxis.—Since several days must elapse after the sensitizing dose is given before the animal becomes sensitized, since the sensitizing material must be of a protein nature, and since anaphylaxis is specific and may be passively transferred, does it not seem reasonable to believe that anaphylaxis is due to antibody formation and is closely related to immunity? That such is the case practically all observers agree. They believe that the sensitizing dose leads to the formation of antibodies which combine with the antigen when it is again introduced into the body, bringing about anaphylactic shock. But why does anaphylactic shock develop in one case and immunity develop in another case under very similar circumstances? According to one theory, the antibodies responsible for anaphylaxis split the antigen into a poisonous and a nonpoisonous portion, and the poisonous portion brings about the anaphylactic symptoms. According to another theory, the antibodies responsible for anaphylaxis are not cast into the blood stream, as are those responsible for immunity, but remain attached to the body cells where the combination with antigen takes place and the injury to the cells brought about by the combination leads to the anaphylactic manifestations. According to still another theory, whether immunity or anaphylaxis will occur is a matter of speed, a slow combination of antibody and antigen leading to immunity while a rapid one leads to anaphylaxis. Whatever the mechanism may be, we believe that we are justified in stating that the sensitizing dose of antigen leads to the production of antibodies remarkably alike if not identical with those responsible for immunity, and when the antigen is again introduced into the body the antibodies combine with it to produce anaphylactic manifestations.

In its final analysis *anaphylaxis is due to the contraction of smooth muscle fibers, and the part of the body primarily attacked in a given animal depends on the distribution of smooth muscle fibers in the species.* For instance, in the guinea pig smooth muscle fibers are very plentiful in the lungs which leads to death from closure of the bronchioles, bronchi, etc., while in the rabbit they are very plentiful in

the pulmonary arteries, and when the arteries contract a burden that leads to cardiac failure is thrown on the right side of the heart.

Allergy.—Many conditions have been considered to be of allergic origin. The most important ones are asthma, hay fever, serum sickness, urticaria and other allergic skin eruptions, angioneurotic edema, and certain drug idiosyncrasies. It was once thought that these conditions were hereditary constitutional abnormalities, but it is now believed that their fundamental etiology differs in no way from that of anaphylaxis, except that sensitization occurs naturally instead of being induced artificially. It is true that allergic diseases are more common in some families than in others, but the thing that is inherited is not the disease itself but a special tendency to become hypersensitive. If the disease itself were inherited, all the members of an affected family would have the same condition, for instance, asthma, which is not the case, because one member may have hay fever, another asthma, and still another some type of allergic skin eruption, etc. It is seldom the case that all the members of a family are hypersensitive.

Assuming that allergic diseases are due to natural sensitization, let us explain how an allergic disease is brought about, for instance asthma due to horse dander. A person who has a natural tendency to become hypersensitive comes in contact with an initial dose of horse dander, usually by inhalation, and the dander excites the body cells to produce antibodies that combine with horse dander when it again enters the body, which brings about an asthmatic attack. Of course everyone comes in contact with horse dander at some time in his life, but comparatively few become sensitized. How drugs which are not proteins act as allergens, which are of protein nature, will be explained in connection with drug allergy.

Allergens may reach the body by way of the respiratory or digestive tracts by contact or by placental transmission. Of these routes, by way of the respiratory tract is most common. For sensitization by way of the intestinal tract to oe-

cur, unchanged protein must pass through the intestinal wall to the blood stream. This occurs most often in children and in adults with digestive disturbances. Active sensitization through the placenta may occur when the mother overindulges in protein foods during the gestation period. In some cases a passive sensitization may be transmitted from the mother to the child in utero via the placenta. This type of sensitization does not last long as is the case in the immunity of the newborn, which is transmitted in the same manner. An allergic person is often sensitive to several different allergens. About 7 per cent of people are allergic. They probably represent those who are so easily sensitized that they become sensitized under the natural conditions of life.

Asthma.—Asthma is an allergic condition that is most often due to animal hair, feathers or dander, house dust, foods, bacteria, and certain cosmetics. Of the first group horse dander, chicken feathers, duck feathers, dog hair, cat hair, and sheep wool are specially important. These gain access to the body via the respiratory tract. Important asthma-producing foods are milk and its products, eggs, meat, fish, and cereals.

Hay Fever.—Hay fever is due to sensitiveness to pollens, and the period of attack corresponds to the time of pollination of the offending plant or plants. To be of importance as a hay fever producer a plant must produce a light dry pollen that is easily carried a long distance by the wind. This excuses both goldenrod and roses, which have been accorded an unearned distinction as causes of hay fever. Early spring hay fever is usually due to the pollen of trees. Late spring and early summer hay fever is most often due to grass pollens and more than 80 per cent of the cases of fall hay fever are due to ragweed pollen. The importance of individual trees, grasses, or other plants depends on geographical location, because a plant may be found in abundance in one portion of the country and not grow at all in another.

Perennial hay fever occurs at irregular intervals throughout the year. The most common causes are animal danders,

vegetable powders, house dust, foods, drugs, and perennial pollinating plants.

Serum Sickness.—After the administration of immune serums two types of reaction may be observed. The first type, known as serum sickness, may occur in persons who have never had a previous injection of horse serum and so far as is known are not sensitive to horse proteins. The second type which occurs most often in those who have asthma due to horse proteins or have had a previous injection of horse serum is of infrequent occurrence but is often serious in its manifestations. This type of reaction bears a close resemblance to anaphylaxis in the lower animals and when it follows the previous injection of horse serum, it represents in the human being the establishment of a condition completely analogous to anaphylaxis in the lower animals.

Serum sickness is of common but by no means universal occurrence, and its manifestations are unpleasant but seldom of danger to life. It usually begins from eight to twelve days after the injection of an immune serum and is characterized by a skin eruption; swollen, painful, and stiff joints; enlargement of the lymph nodes; leucopenia, and decreased coagulation of the blood. In some cases manifestations may occur only around the site of injection (local serum disease). It is thought that serum sickness is due to the action of antibodies formed during the early days after the injection on a part of the serum still remaining in the body.

The anaphylaxis-like manifestations following the injection of an immune serum are of infrequent occurrence but are of such a serious nature that an immune serum should be administered with extreme caution to asthmatic patients and to those who have had a previous injection of horse serum. In all cases tests to detect sensitivity to horse serum should be done before an immune serum is given, because the factor that is responsible for untoward reactions is the horse serum which forms the basis of practically all antitoxins and immune serums. Anaphylaxis-like symptoms due to the previous injection of an immune serum are most

likely to occur when the second injection is given two or three weeks after the first, but more or less severe reactions may occur when a second injection is given months or years after the first. The anaphylaxis-like state is most likely to occur in man after intravenous or other rapid method of injection of the serum. In some cases anaphylaxis-like manifestations may be so severe as to lead to immediate collapse or

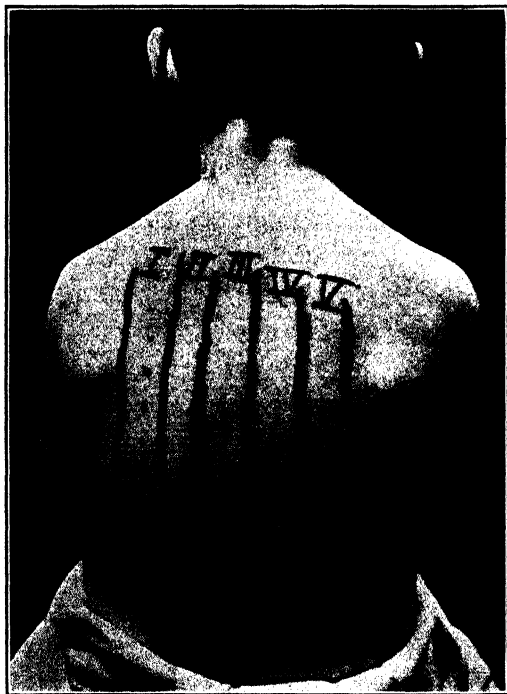


Fig. 68.—Tests for hypersensitiveness on back of a child. Six test materials have been placed in column I. The skin is marked off in columns in order to facilitate recording the tests.

death. Fortunately this is of extreme rarity. Characteristic manifestations are fall in blood pressure, drop in body temperature, and respiratory embarrassment. In order to guard against reactions, should an immune serum have to be given later, it is advisable to use toxin-antitoxin prepared with goat serum antitoxin or toxoid in establishing an active immunity to diphtheria in children.

Bacterial Allergy.—Repeated infections or chronic infections may render a patient hypersensitive to the bacteria causing the infection. This is well illustrated in tuberculosis, in which case the patient becomes allergic to *Myco. tuberculosis* or its products and gives a positive reaction when an extract of *Myco. tuberculosis* is applied to the skin. This is the basis of the tuberculin reaction used in the diagnosis of tuberculosis. Patients may likewise become sensitive to other organisms such as *Brucella* (the causative agents of undulant fever), streptococci, etc. Some workers believe that the manifestations of acute rheumatic fever are due to an allergic reaction to streptococci.

Urticaria and Allergic Skin Eruptions.—These allergic conditions may be due to foods or other allergens. The mechanism of their production is not well understood.

Sensitivity to Drugs.—It is rather common to find a person who exhibits untoward symptoms upon taking certain drugs, such as quinine, morphine, strychnine, etc. It is believed that when these drugs are habitually brought in contact with the body proteins of certain persons a chemical combination between the drug and certain of the body proteins takes place, forming a protein compound foreign to the body against which the body cells produce antibodies. It is well known that when antibodies are formed against an antigen, they may subsequently react with a portion of the antigen, for instance the nonprotein portion of certain bacteria. Upon these premises it is assumed that the antibodies formed against the drug-protein combination attacks the drug alone when it enters the body.

Sensitivity to the sulfonamide drugs is a not uncommon condition. It seems more likely to occur when the drugs are used in the form of ointments. Sensitivity to penicillin may occur. The manifestations of sensitivity to penicillin usually take the form of an eruption or some other condition of the skin.

Hypersensitiveness to Vaccines.—The administration of certain vaccines, such as yellow fever vaccine, some types of Rickettsial vaccines and influenza virus vaccines which are grown in chicken embryos or yolk sacs may bring about a

hypersensitive reaction in persons allergic to egg or chicken. It is also conceivable that repeated injection of one of these vaccines might lead to sensitization and subsequent hypersensitive reaction.

Laboratory Tests to Detect Hypersensitiveness.—If some of the antigen to which a person is sensitive is rubbed in a scratch on the skin or some of the dilute antigen is injected between the layers of the skin, a wheal from 0.5 to 2 cm. in diameter will occur at the site of contact within twenty to thirty minutes. If the person is not sensitive to the antigen, no reaction will occur. The ophthalmic test is of value in detecting sensitization to serum. A drop of the *diluted* serum is instilled into the conjunctival sac; and if the patient is sensitive to horse serum, redness of the conjunctiva and a watery discharge will appear within ten to twenty minutes. The reaction may be controlled by epinephrine. The “*patch*” test is useful in detecting the cause of *contact dermatitis* which is a local allergic condition brought about by substances coming in direct contact with the skin. Such substances are fabrics, furs, cosmetics, drugs, chemicals, etc. In this test the material is applied directly to the skin and held in place by means of adhesive tape from one to four days. A positive reaction reproduces the lesion from which the patient is suffering with vesicle and papule formation.

Desensitization.—In some cases desensitization may be accomplished by giving repeated injections of very small amounts of the antigen to which the patient is sensitive. For instance, a patient hypersensitive to horse serum may be given an immune serum if the injection is preceded by several injections of very small amounts at thirty-minute intervals. The desensitizing doses are graded by the reaction of the patient, and the administration of an immune serum to a hypersensitive person should be undertaken only by those with experience in immune therapy. A similar but much prolonged method of desensitization is used in the treatment of hay fever and selected cases of asthma and urticaria. Desensitization, unlike sensitization, is of relatively short duration.

Question for Review

1. Briefly discuss hypersensitiveness to vaccines.

True-False Test

Place the word "true" or "false" before each statement.

- 1. By anaphylaxis is meant the hypersensitiveness produced in animals by artificially introducing into their bodies substances capable of bringing about a hypersensitive state.
- 2. Using a hypersensitive donor for blood transfusion may render the recipient hypersensitive.
- 3. Anaphylaxis is not due to antibody formation.
- 4. Anaphylactic symptoms depend entirely upon the distribution of striated muscle in the species.
- 5. In order for anaphylaxis to occur, the sensitizing and provocative doses must be of the same substance.
- 6. In allergy the sensitization occurs by having the substance introduced artificially.
- 7. Allergic diseases may be inherited.
- 8. Immune serum should be administered with extreme caution to asthmatic patients and to those who have had a previous injection of horse serum.
- 9. It is thought by some that the manifestations of acute rheumatic fever are due to an allergic reaction to streptococci.

Completion Test

1. Hypersensitiveness occurs in two forms: ----- and -----.
2. Allergy-producing agents may reach the body by way of the -----, -----, or by -----.
3. Hay fever is usually due to sensitiveness to -----.
4. Asthma is an allergic condition that is most often due to: -----, -----, or -----.
5. Discuss two types of reactions that may occur following the injection of immune serums. Which is most common? Which is most dangerous?
6. What is the basis of the tuberculin reaction used in the diagnosis of tuberculosis?
7. Man may be sensitive to certain drugs such as -----, -----, or -----.
8. Three types of tests to detect hypersensitiveness are -----, -----, and -----.
9. How may desensitization be accomplished?

References

- Sherwood, N. P.: Immunology, St. Louis, 1941, The C. V. Mosby Co.
- Zinsser and Bayne-Jones: Textbook of Bacteriology, New York, 1939,
D. Appleton-Century Co.
- Topley and Wilson: Principles of Bacteriology and Immunology,
Baltimore, 1946, Williams & Wilkins Co.
- Vaughan, W. T.: Practice of Allergy, St. Louis, 1948, The C. V.
Mosby Co.
- Jordan, Edwin O., and Burrows, William: Textbook of Bacteriology,
Philadelphia, 1945, W. B. Saunders Co.

CHAPTER XIX

HOW COMMUNICABLE DISEASES ARE TRANSMITTED

The causative agents of communicable diseases may be transmitted from the source of infection to the recipient of the infection by (1) direct contact, (2) indirect contact, or (3) insect carriers. The source of infection may be (1) an animal or person ill of the disease or (2) a human or animal carrier.

Direct contact is the term applied when an infection is spread more or less directly from person to person. It does not necessarily mean actual bodily contact but does indicate a rather close association. For the spread of some diseases, however, actual bodily contact is necessary. Notable examples of this type of diseases are syphilis and gonorrhea. *Droplet infection*, which means infection by bacteria cast off in the fine spray from the mouth and nose during coughing, talking, laughing, etc., is a form of direct contact. Another form is by placental transmission (see page 181). The diseases most often spread by direct contact are tuberculosis, diphtheria, measles, pneumonia, scarlet fever, colds, smallpox, syphilis, gonorrhea, and epidemic meningitis. Some of these may be transmitted also by indirect contact.

Indirect contact refers to the spread of the causative agent of a disease by such conveyers as milk and other foods, water, air, contaminated hands, and inanimate objects. The diseases most commonly spread in this manner are those in which the infectious material enters the body via the mouth. Diseases of this type are typhoid fever, paratyphoid fever, amebic dysentery, bacillary dysentery, cholera, septic sore throat, and scarlet fever. Scarlet fever, however, is most often spread by direct contact. A long time ago it was thought that many infections were conveyed from person to person by the air. Later it became generally believed that air-borne infections were of little consequence. More recent

studies seem to have re-established the importance of air as a bearer of infection because it has been proved that particles of dried droplets from the mouth or nose or very small droplets which have dried may be kept in the air for a considerable time and carried a rather long distance. Naturally it is the respiratory infections in which the transfer by way of the air is of greatest importance. Among the methods used to control air-borne infections are oiling of floors and bed clothing, ultraviolet light, and aerosols.

That the importance of contaminated fingers as conveyers of infection may be properly stressed, we present in the form of an outline the various sites from which and to which they may transfer disease-producing agents.

1. From one part to another part of the body of the owner of the fingers.

2. From the body of the owner of the fingers to a second person.

3. From the body of the owner of the fingers to food, drink, materials, or objects that become sources of infection.

4. From the body of an infected person to the body of the owner of the fingers.

5. From contaminated food, drink, materials, or objects to the body of the owner of the fingers.

6. From contaminated foods, drinks, materials, or objects to the body of another person.

7. From an infected person to a third person.

8. From the body of an infected person to foods, drinks, materials, or objects that become sources of infection.

Insects act as conveyers of disease mechanically or biologically. In the former case they merely get the organisms causing a disease on their feet or other parts of their body and carry them from place to place. Flies often transfer the causative agents of typhoid fever and dysentery from the excreta of patients to foods in this manner, and their feet often become contaminated with tubercle bacilli when they light on infected sputum. They act as more or less important carriers of more than twenty other diseases. The distance that flies may carry infection is considerable, because they have been known to travel miles in search of

food. In the biological transfer of disease, the insect bites a person or animal ill of a disease or a carrier and ingests some of the infected blood. The organisms or virus taken in with the blood undergo a cycle of development within the body of the insect; and after the period of development, which requires a definite length of time, the insect is capable of transferring the infection to a well person, usually by biting. Diseases that are spread in this manner are malaria, yellow fever, and dengue fever spread by mosquitoes; typhus fever transmitted by lice; Texas fever (a disease of cattle) spread by ticks; African sleeping sickness spread by the tsetse fly, and plague spread by fleas. As a rule, a particular infection is spread by only one species of insect, and a given insect is able to spread only one type of infection. There are, however, important exceptions to this rule.

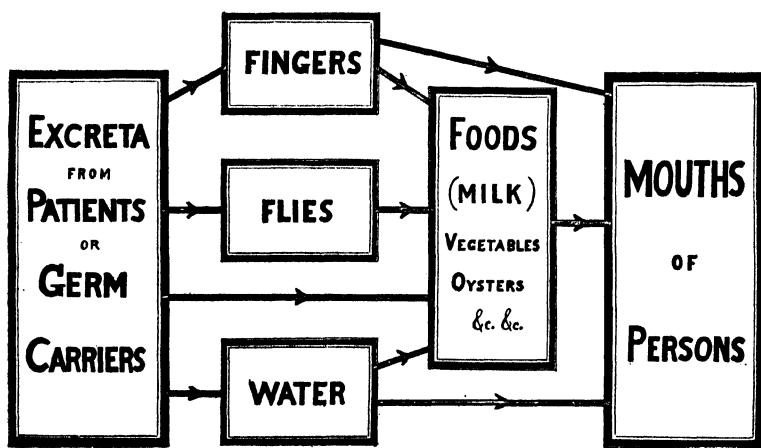


Fig. 69.—Illustration of the modes by which typhoid fever may be spread (From U. S. P. H. S.) (From Boyd, M. F.: *Preventive Medicine*. W. B. Saunders Co.)

For diseases that are biologically transferred to be prevalent in a community both the transmitting insect and hosts who harbor the infection must be present in the community.

Human carriers are persons who harbor pathogenic agents in their bodies but show no signs of illness. This is because carriers are usually immune to the diseases that they

spread. *Convalescent carriers* are those who harbor an organism during recovery from an illness brought about by the organism. *Passive carriers* are those who harbor a pathogenic organism without having had the disease which the organism causes. *Active carriers* are those who harbor an organism for a long time after recovery from an illness due to the organism. *Intestinal* and *urinary carriers* are those who discharge the infectious agent from the body via the feces and urine, respectively. *Oral carriers* discharge infectious material by way of the mouth. As a rule, an actual case of a disease is more likely to spread infection to others than is a carrier. Carriers and unrecognized cases keep epidemic diseases in existence during interepidemic periods. It has been found that just before epidemics of certain diseases, notably diphtheria and meningitis, the number of carriers increases. Human carriers play an important part in the spread of diphtheria, epidemic meningitis, typhoid fever, paratyphoid fever, amebic dysentery, bacillary dysentery, streptococcus infections, and pneumonia. The importance of carriers in the spread of a disease depends on the frequency with which people become carriers of the disease and the time the carrier state persists.

Animals frequently spread diseases to man. Rabies is acquired by being bitten by rabid dogs, cats, or other animals. Children often contract tuberculosis by drinking the raw milk of infected cows. Bubonic plague is primarily a disease of rats that is transmitted from rat to rat and from rat to man by the flea. Undulant fever may be transmitted to man by milk, or it may be acquired by handling the meat of infected animals. Tularemia is contracted from rodents, especially wild rabbits. Psittacosis is an infectious disease of parrots that is transmitted from the sick parrot to man. Typhus fever is primarily a disease of rats that is transmitted from rat to rat by rat lice and fleas and from man to man by lice. Those handling the hides of anthrax-infected animals may contract the disease. Tetanus may be indirectly contracted from horses because the tetanus bacillus is a normal inhabitant of the intestinal canal of the horse.

This is why wounds contaminated by barnyard dirt are more likely to be followed by tetanus than others.

Fomites refer to inanimate objects that may act as spreaders of infection. The most important spreaders of this type are handkerchiefs, towels, pencils, and drinking cups.

Food other than milk may act as a source of infection. Typhoid fever, paratyphoid fever, dysentery, and cholera may be spread by way of contaminated food. Botulism is most often caused by eating insufficiently heated canned foods. Trichinosis and tapeworms are contracted by eating insufficiently cooked meats.

Certain diseases are primarily diseases of filth. Of these typhus fever as it occurs in certain parts of the world is an example. However, filth plays little or no part in the spread of typhus fever in the United States. It might be mentioned that neither does the disease occur in epidemic form in this country. People who are uncleanly in their habits are more likely to contract an infectious disease than those who are not and the disease is more difficult to control in an unsanitary community.

For the continuous existence of a disease there must be some *reservoir of infection*. In only a few diseases does the causative agent live in lifeless surroundings outside the body long enough to become a continuous source of infection. It is now believed that the most important reservoirs of infection are human or animal cases or carriers. Plants may be the reservoir of infection in some of the mycoses.

Questions for Review

1. Discuss the importance of contaminated fingers as conveyers of infection.
2. Name some diseases spread by lower animals; also name the animal transmitting them.

True-False Test

Place the word "true" or "false" before each statement.

- 1. Direct contact is the term applied when an infection is spread only by direct body contact.
- 2. Indirect contact refers to the spread of the causative agent of a disease by such conveyers as milk, contaminated hands, and inanimate objects.

- 3. Scarlet fever is most often spread by indirect contact.
- 4. Flies act as carriers of more than twenty diseases.
- 5. Active carriers are those who harbor an organism during recovery from an illness brought about by the organism.
- 6. A carrier is more likely to spread infection than the actual case.

Completion Test

1. Communicable diseases may be spread by the following methods:
-----,
or -----.
2. Diseases most often spread by direct contact are -----,
-----,
-----,
-----.
3. Insects act as conveyers of disease ----- or -----.
4. ----- are persons who harbor pathogenic agents in their bodies but show no signs of illness.
5. ----- are those who harbor an organism during recovery from an illness brought about by the organism.

References

- Zinsser and Bayne-Jones: Textbook of Bacteriology, New York, 1939, D. Appleton-Century Co.
- Rosenau, Milton J.: Preventive Medicine and Hygiene, New York, 1935, D. Appleton-Century Co.
- Boyd, Mark F.: Preventive Medicine, Philadelphia, 1945, W. B. Saunders Co.
- Sharp, William B.: Practical Microbiology and Public Health, St. Louis, 1938, The C. V. Mosby Co.
- Jordan, Edwin O., and Burrows, William: Textbook of Bacteriology, Philadelphia, 1945, W. B. Saunders Co.
- Control of Airborne Infections: Editorial, J. A. M. A. 129: 552, 1945.
- Hart, Deryl: The Importance of Airborne Pathogenic Bacteria in the Operating Room, J. A. M. A. 117: 1610, 1940.
- Robertson, Hamburger, Loosli, Puck, Lemon, and Wise: A Study of the Nature and Control of Airborne Infections in Army Camps, J. A. M. A. 126: 993, 1944.

SECTION III

BACTERIOLOGY OF WATER AND MILK

CHAPTER XX

WATER, SWIMMING POOLS, SEWAGE

Practically all waters under natural conditions contain bacteria. Some contain many bacteria; others contain few or none. These bacteria may be harmless water bacteria, among which are nitrifying and nitrogen-fixing bacteria, bacteria from the soil, bacteria from the air, or bacteria from the excreta of man or animals. The number and kind of bacteria present depend on the source of the water and its exposure to pollution with the excreta of man or animals or other contaminated material.

Since sewage contains the pooled excreta from those who are sick as well as from those who are well, it necessarily must often contain pathogenic organisms, especially those which leave the body by the feces or urine. Sewage must be properly disposed of in order to avoid contamination of water supplies or the spread of its bacterial content by flies or other agencies.

Diseases Spread by Water.—The diseases spread by water are usually those whose causative organisms leave the body by way of the alimentary tract, and water-borne infections are usually contracted by drinking contaminated water. Most important of the diseases that may be spread by water are typhoid fever, bacillary dysentery, amebic dysentery, paratyphoid fever, and cholera. Pathogenic bacteria do not live for a long time in water and do not multiply there. They live longer in water that is cool and contains considerable organic matter. They rapidly die in ice. When a water-borne epidemic occurs, most cases occur within a few days, indicating that all were infected at about the same time.

Sources of Water.—From a sanitary standpoint water may be classified as (1) rain or snow water, (2) surface water (shallow wells, rivers, ponds, lakes, waste water, etc.), and (3) ground water (deep wells and springs). As a general rule, surface water contains more bacteria than either ground or rain water, and ground water contains more than rain water. Surface water contains many harmless bacteria from the soil and in the vicinity of cities is often contaminated with sewage bacteria. Unless they are properly constructed, shallow wells may become contaminated with the drainage from outhouses, stables, etc. Improperly constructed shallow wells have been responsible for many outbreaks of typhoid fever and dysentery in rural communities. For a shallow well to be safe, its upper portion must be lined with an impervious material so that water from the surface will not seep into it, and it should be located so that outhouses drain away from it. Of course it should be kept tightly closed. Shallow springs may be just as dangerous as shallow wells. Deep well water and deep spring water usually contain few bacteria because they are filtered out as the water trickles through the layers of the earth but, like shallow wells, deep wells must be protected against pollution with surface water. In this connection it should be remembered that bacterial pollution may occur when a well is situated within 200 feet of the source of pollution, and chemical pollution may occur for a distance of 400 feet. Pollution is more likely to occur during wet weather. Surface water in sparsely settled localities may be comparatively safe, but the only safe rule is not to use surface water without purification.

Bacteriological Examination of Water.—Experience has taught that it is almost impossible to isolate from water the organisms that are responsible for the most important water-borne diseases because there are relatively few to begin with and they do not multiply in water. Sanitarians and public health workers, therefore, came to the conclusion that the only safe method of protecting the population from water-borne diseases was to condemn any water showing fecal pollution as being unfit for human use on the ground that it *might* contain harmful organisms which, as we have already

learned, practically always gain access to water by way of the feces (or in some cases the urine) of man. Whether fecal pollution exists or not is determined by examining the water

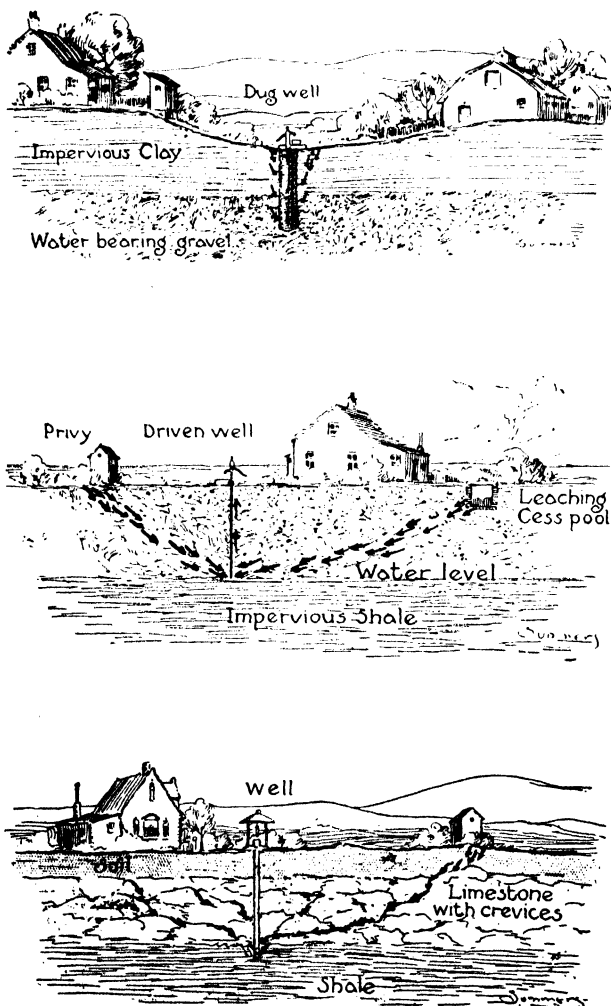


Fig. 70.—Diagram showing methods by which a well may become contaminated. (From Gardner: *Practical Sanitation*. The C. V. Mosby Co.)

for colon bacilli which occur in abundance in feces. Since colon bacilli may originate from sources other than feces, they must be proved to be of fecal origin before their pres-

ence in a sample of water can be accorded any sanitary significance. This can be done by comparatively simple laboratory tests. European bacteriologists have devised systems whereby the water is not examined for colon bacilli but for *Streptococcus faecalis* or *Clostridium welchii*, both of which are just as constantly present, but not so plentiful, in the feces as colon bacilli.

Drinking Water Standards.—The United States Treasury Department has adopted certain standards for drinking and culinary water used in interstate commerce. These to a great extent have served as standards throughout the country. Included within these standards are specifications relating to (1) source and protection of the water, (2) its physical and chemical properties, (3) its bacteriological quality, and (4) its distribution. According to these standards colon bacilli may be found in a certain proportion of the samples without necessarily indicating that the water is unsuitable for drinking and cooking purposes. The interpretation of a bacteriological water analysis depends on the source of the water and the number of colon bacilli present.

Water Purification.—Water may become purified by natural or artificial means. As water trickles through the earth, bacteria are filtered out. Water standing in lakes and ponds undergoes some degree of purification. This is due to the combined action of sunlight, sedimentation, dilution of the impurities, and destruction of bacteria by protozoa. Streams have a tendency to become purer as they flow along, but so many factors come into play and the possibility of polluted material being added to the stream as it flows along is so great that the self-purification of streams is not to be relied upon at all. In fact, all of the methods of natural purification mentioned above are slow and uncertain in their action and, as we have already been told, the only safe method is to regard all surface waters not subjected to artificial purification as being potential sources of danger.

The methods of artificial water purification are: (1) clarification and sedimentation, (2) filtration, and (3) chemical treatment. In clarification and sedimentation the water is

held for several hours in a large sedimenting basin during which time the larger particles of suspended matter settle to the bottom. If a large amount of suspended matter is present, alum is added to the water; this causes coagulation and carries the suspended matter to the bottom. After clarification and sedimentation are complete, the water is subjected to filtration. Filters are so constructed that their upper layers are made of sand and their lower layers are made of coarse gravel. Facilities are provided for draining the water away after it has been passed through the

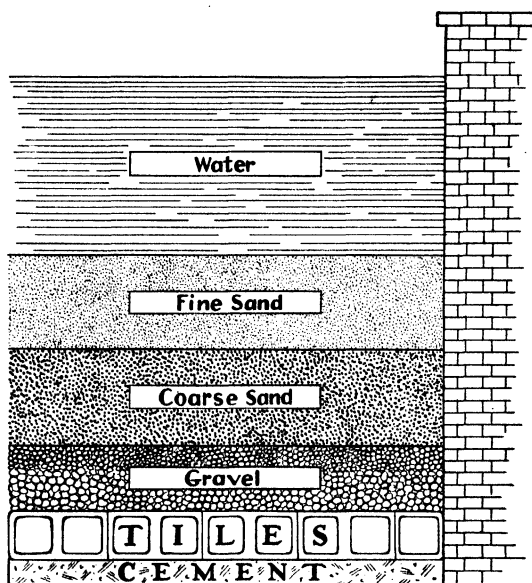


Fig. 71.—Cross-section through a slow sand filter. The water soaks through the fine sand, the coarse sand, and the gravel, entering the open tiles which carry it to a collecting basin. (From Turner-McHose: Effective Living, The C. V. Mosby Co.)

filter. The efficiency of a filter depends on the formation of a gelatinous scum over its surface. This scum is due to the natural settlings from the water or the precipitation brought about by the addition of alum to the water. Efficient filtration removes all pathogenic and most saprophytic organisms. After filtration, water is often chemically treated.

Chemicals which may be added to water to purify it are lime, chlorine, ozone, alum, and copper sulphate. Of these,

chlorine is most often used. To be effective it must be present in a concentration of 0.5 to 1 part per million parts of water. Copper sulphate is used chiefly to destroy algae. For this purpose it is used in a concentration of one part per million parts of water. If the water does not contain an excess of organic matter one part of copper sulphate to 400,000 parts of water will destroy typhoid bacilli. The use of alum has been described above.

Purification of Sewage.—Many methods of sewage purification are in use. The procedures involved are screening or sedimentation to remove the larger particles, chemical treatment to remove small particles, bacterial action which brings about liquefaction and purification, aeration, to bring about oxidation, and filtration through sand. In a general way the decay of the material which goes to make sewage is like the decay of other organic material.

Swimming Pool Sanitation.—Swimming pools may convey such diseases as conjunctivitis, ear infections, skin diseases, intestinal infections, etc., unless kept in a sanitary condition. The source of infection is usually the people using the pool. Swimming pool water should be kept in the same state of purity as drinking water. This is done by frequent changing of the water and the use of disinfectants. Chlorine is the disinfectant of choice. The highest concentration possible should be maintained. This is about 0.5 part of chlorine to one million parts of water. A higher concentration is irritating to the eyes. Ultraviolet light may be used. Suits and towels used by the bathers should be sterilized. Before entering the pool, each person should be required to take a shower bath using soap and to bathe the feet in 15 per cent sodium thiosulphate. The latter prevents fungus infections of the feet. Persons who have infections of any kind should not be allowed to use the pool.

True-False Test

Place the word "true" or "false" before each statement.

- 1. The number and kind of bacteria present in water depend on the source of the water and its exposure to pollution with the excreta of man or animals.
- 2. Pathogenic bacteria will live for a long time in water.

- 3. Improperly constructed shallow wells have been responsible for many outbreaks of typhoid fever and dysentery in rural communities.
- 4. Bacteria that are responsible for the most important water-borne diseases are easily isolated from water.
- 5. Water may become purified by natural or artificial means.
- 6. Swimming pool water should be kept in the same state of purity as drinking water.

Completion Test

1. Some of the most important diseases that may be spread by water are _____, _____, _____, _____ and _____.
2. As water trickles through the earth, _____ are filtered out.
3. In making a bacteriological water analysis, the water is examined for _____.
4. Three methods of artificial water purification are _____, _____, and _____.
5. Chemicals which may be added to water to purify it are _____, _____, _____, and _____.
6. Swimming pools may convey such diseases as _____, _____, _____, _____, and _____.
7. Discuss the purification of sewage.

References

- Rosenau, Milton J.: *Preventive Medicine and Hygiene*, New York 1935, D. Appleton-Century Co.
- Boyd, Mark F.: *Preventive Medicine*, Philadelphia, 1945, W. B. Saunders Co.
- Manual of Recommended Water Sanitation, Practice: Public Health Reports 58: 69-122, 1943.*
- Smillie, Wilson G.: *Preventive Medicine and Public Health*, New York, 1946, The Macmillan Co.
- Prescott, Winslow, and McGrady: *Water Bacteriology*, New York, 1946, John Wiley & Sons, Inc.
- Public Health Service Drinking Water Standards 1946: Pub. Health Rep. 61: 371-384, 1946.*

CHAPTER XXI

MILK AND FOOD

I. MILK

If obtained in a pure state and kept pure, milk is our best single food. If improperly handled, it is our most dangerous food. The reason that milk is such an important conveyer of infection is that it is an excellent culture medium and is consumed uncooked.

Bacteria in Milk.—Milk as secreted by the mammary glands of perfectly healthy cows is usually sterile, but during milking it becomes contaminated with bacteria from the teats and milk ducts so that by the time it enters the pail contamination has taken place. Under the very best conditions the bacterial content of milk is relatively high. These bacteria are of two classes: those which are so commonly present, even though they come from external sources, as to be regarded as normal milk bacteria; and those which are pathogenic. The former aid in the souring of milk but may destroy its value as a food; the latter cause disease.

Bacteria gain access to milk by many different routes. They may be present in the udders of unhealthy cows and are found in the milk ducts and teats of healthy cows. Unclean milking utensils, pasteurizing tanks and milk bottles, dust, manure, etc., are important sources of contamination. The most important sources of the pathogenic bacteria found in milk are the people who handle the milk and the milk from infected cows. As soon as bacteria gain access to milk, they begin to multiply. This can be prevented by rapidly chilling the milk as soon as it is milked and keeping it cold.

The organisms most commonly found in milk are micrococci and streptococci, the lactic acid organisms which are responsible for the souring of milk, and certain members of the colon group.

Although it is not the only criterion, the number of bacteria in milk is the best index of its sanitary quality. The

number present depends on the number originally introduced into the milk and the temperature at which the milk is kept. If cooled to 10° C. or lower as soon as milked and kept at that temperature, no great increase in the number of bacteria will occur, but if the milk is allowed to become warm, a rapid increase will take place. Milk of high quality may contain only a few hundred bacteria per cubic centimeter. Bad milk may contain millions of bacteria per cubic centimeter. All authorities agree, however, that a single high bacteria count does not necessarily mean that the milk is of poor quality and that to be of significance a high bacteria count must occur day after day.

Diseases Transmitted by Milk.—The diseases most often spread by milk are typhoid fever, bacillary dysentery, scarlet fever, infantile diarrhea, septic sore throat, undulant fever, and bovine tuberculosis. The spread of typhoid fever, bacillary dysentery, scarlet fever, and septic sore throat by milk is usually due to contamination of the milk by the discharges of a handler who is ill of the disease or is a carrier. At the present time milk-borne epidemics of typhoid fever are more common than water-borne ones. Bovine tuberculosis, especially in children under five years of age, is usually due to the ingestion of the milk of tuberculous cows. In cattle tuberculosis most often affects the lungs, but the sputum is swallowed and excreted in the feces. As a rule, the bacilli get into the milk by fecal contamination, but in some cases the udder becomes infected and the bacilli are excreted in the milk. Undulant fever may be contracted by drinking the milk of infected animals. One type is contracted by drinking the milk of infected goats; the other is contracted by drinking the milk of infected cows. The saprophytic bacteria of milk may contribute to the infantile diarrheas of the summer months. Diphtheria is occasionally spread by milk. Let it be remembered that the diseases mentioned above are not spread by milk alone.

Characteristics of Milk-Borne Epidemics.—Characteristic of milk-borne epidemics is the occurrence of the majority of cases among the patrons of a certain dairy. A person ill of the disease or a carrier is often found among the per-

sonnel of the dairy. In 1927 a milk-borne epidemic of typhoid fever in Montreal gave rise to 4,755 cases and 453 deaths. More than fifty milk-borne epidemics of septic sore throat have been reported since 1908.

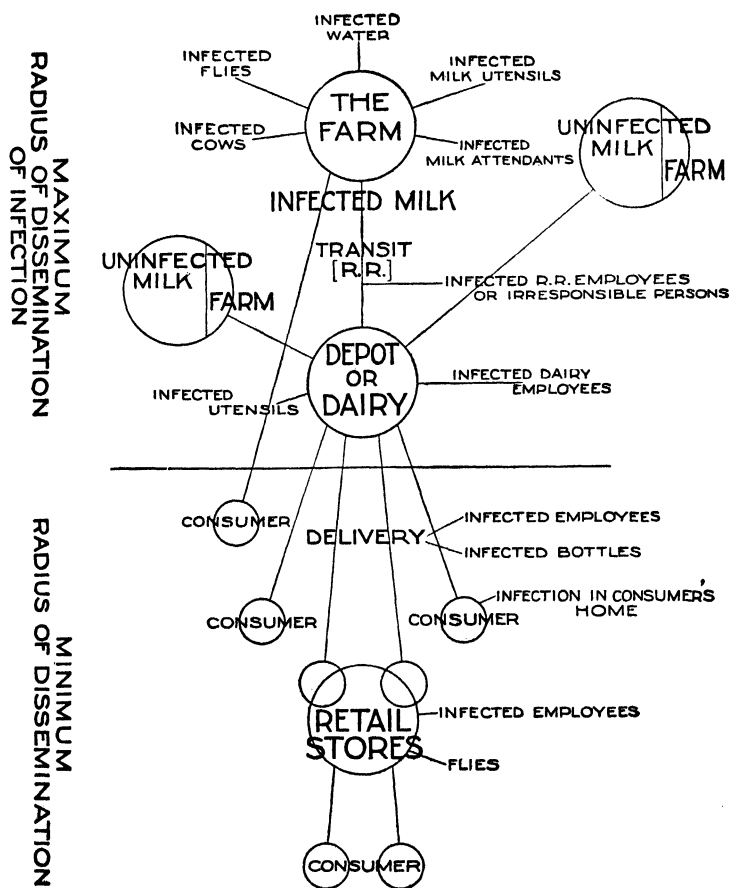


Fig. 72.—Diagram showing how milk may become contaminated and spread infection. (From Boyd, M. F.: *Preventive Medicine*. W. B. Saunders Co.)

Pasteurized Milk.—Commercial milk is of two types: raw or unheated milk and pasteurized milk. Pasteurized milk is milk that has been heated for a short time to a temperature high enough to kill all nonspore-bearing pathogenic bacteria but not high enough to affect the chemical com-

position of the milk. The Commission of Milk Standards of the New York Milk Committee recommends that milk be heated to a temperature of from 140° F. (60° C.) to 155° F. (68° C.). At 140° F. the time of exposure should be at least twenty minutes and for each degree above 140° F. the time may be reduced one minute, but in no case can the time of exposure be less than five minutes. The milk should be constantly stirred while it is being pasteurized and should be transferred through pipes, where it is chilled,



Fig. 73.—Modern pasteurizing plant. This plant consists of a heater (shown at back) and four tanks. The milk is heated to the required temperature by the heater and then transferred to the tanks where the heat is maintained for the required time. Heat is controlled and valves are operated electrically from the panel in the foreground. The capacity of this plant is 7,000 pounds per hour. (Courtesy of the Creamery Package Mfg. Co.)

to the bottling machines. It should be bottled in sterile bottles. We should not get the impression that pasteurization completely sterilizes milk, and it should not be used as a substitute for the sanitary handling of milk.

Milk Grading.—Different states have different systems of grading their milk supply. As a rule, grading is based on the sanitation of the dairy, the health of the cows, methods of handling the milk, the chemical composition of the milk,

and its bacterial content. The American Public Health Association offers the following method of grading:

Grade A (raw).—Cows should be free of disease and the employees of the dairy should not be ill or carriers of disease. The bacteria count should not exceed 10,000 per cubic centimeter at the time of delivery.

Grade A (pasteurized).—Cows should be free of disease and the milk should be handled in such a manner that the bacteria count does not exceed 200,000 per cubic centimeter before pasteurization or 10,000 living bacteria after pasteurization.

Grade B (pasteurized).—Cows should be free of disease and the bacteria count of the milk should not exceed 1,000,000 per cubic centimeter before pasteurization or 50,000 living bacteria after pasteurization.

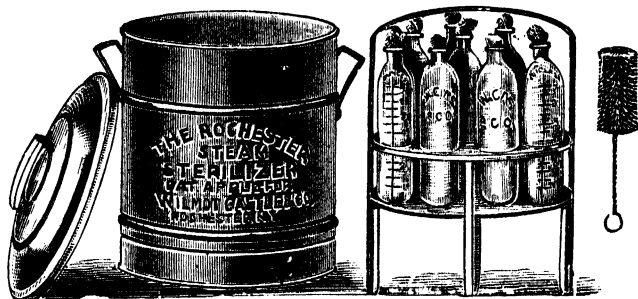


Fig. 74.—Outfit for home pasteurization of milk. (Courtesy of Wilmot Castle Co.)

Grade C.—Milk from healthy cows which is produced under such conditions that the bacteria count exceeds 1,000,000 per cubic centimeter. This milk should be pasteurized or boiled and should contain less than 50,000 living bacteria per cubic centimeter when delivered. This milk should be used only for manufacturing and cooking.

Certified Milk.—Certified milk is milk produced in accordance with the specifications of the American Association of Medical Milk Commissions. The supervision of the production of certified milk in each community is in the hands of a committee of at least five members appointed by a recognized state, county or city medical society.

Pasteurized Versus Raw Milk.—Pasteurization is the most important single item in the establishment of a safe milk supply. Pasteurization, however, should never be used as a cover for negligence in general cleanliness. Some of the objections to pasteurization that have been made are that it destroys vitamins, that dairymen may not be as careful when they know that the milk is to be pasteurized, and that pasteurization may be carelessly and ineffectively done. The latter two objections can be overcome by a thorough system of inspection. The lack of vitamins, if it is true that they are destroyed, would affect only small children and this could be remedied by feeding fruit juices, etc. Pasteurization does not produce the pronounced changes in milk that higher heat (boiling) does, such as decomposition of proteins, changes in the phosphorus content, precipitation of calcium and magnesium, expulsion of carbon dioxide, burning of sugar, and the destruction of ferments.

Requirements for a Safe Milk Supply.—To insure a safe milk supply the following requirements must be met:

1. The cows must be free from tuberculosis or other diseases.
2. All persons handling the milk must be free from the organisms of infectious disease and their hands and persons must be kept clean.
3. The premises should be kept clean.
4. The udders and flanks of the cows should be washed before milking.
5. Milk pails should have narrow openings.
6. The milking utensils and machinery that come in contact with the milk should be kept sterile and should be so constructed as to prevent the access of dust and flies.
7. The milk should be chilled to 10° C. or lower as soon as milked and kept cold.
8. It should be pasteurized and again chilled.
9. It should be bottled in sterile bottles.
10. It should be kept cold by delivering in refrigerated trucks and should be placed in the refrigerator when delivered in the home.

II. FOOD

A. Diseases Transmitted by Food

(See page 237)

B. Food Poisoning

Food Poisoning.—In addition to being an agent by which bacterial infection is spread, food may be a cause of food poisoning which is defined as an acute illness brought about by some injurious agent ingested in food. It may be bacterial or nonbacterial in origin. Bacterial food poisoning may be due to the action of ingested toxins (food intoxication) or multiplication of ingested bacteria (food infection). Food intoxication is due to staphylococci or *Cl. botulinum*. The latter will be discussed in a subsequent chapter. Food infection is due to members of the paratyphoid group of organisms. Food poisoning, especially food infection and intoxication due to staphylococci, was formerly known as ptomaine poisoning. This is incorrect because ptomaines play no part in food poisoning.

Food infection, as has been said, is due to the multiplication of bacteria that have been taken into the intestinal canal and the responsible bacteria are members of the paratyphoid group. Once inside the canal they multiply rapidly and bring about a widespread inflammation with severe symptoms. The symptoms are those of an acute intestinal inflammation; namely, nausea, vomiting, diarrhea, and fever. The incubation period is from six to twelve hours and the death rate is about 2 per cent. The insufficiently cooked meat of infected animals may convey the disease to man, but in most cases the organisms reach the food, which is usually but not necessarily meat, from outside sources. Such sources are the intestinal contents of the slaughtered animal, the intestinal contents of animals (especially rats and mice) that have come in contact with the food and, what is probably most important of all, human carriers of the bacteria. Foods cooked in large quantities are more often the source of infection than foods cooked in small quantities. This is because heat is not as likely to penetrate and sterilize a large quantity of food as a small one. Prevention depends on cleanliness in hand-

ling food, the detection of carriers, the proper cooking of food, and the proper refrigeration of food that has been cooked.

Staphylococcus food intoxication appears to be due to the action of an enterotoxin liberated by staphylococci. Its incubation period is short, from two to six hours. The symptoms are not marked by extreme severity and recovery occurs in from twenty-four to forty-eight hours. It usually follows the ingestion of starchy foods, especially potato salad, custards, pies, etc.

Characteristic of food infections and intoxications is that when several persons eat the offending food, many of them are attacked.

C. Food Preservation

There are numerous methods of preserving food. The following are a few of them:

1. *Drying*—The bacteria are unable to multiply on account of lack of water.

2. *Smoking*—The food is dried and preservatives from the smoke added to it.

3. *Pickling*—The high acid content of the medium prevents bacterial multiplication.

4. *Preserving in brine and salting*—The osmotic pressure of the medium is so changed that bacteria will not multiply. In some cases water is extracted from the bacterial cell.

5. *Canning*—Bacteria and other microorganisms are destroyed by heat and the food hermetically sealed, which prevents the access of bacteria. The sealing also excludes free oxygen which supports the growth of molds, yeasts, and most species of pathogenic bacteria.

6. *Preserving*—The food is heated and sugar is added. A large amount of sugar retards bacterial multiplication in the same manner as salt. However, it does not retard the multiplication of molds. Heating and sealing have the same effect as in canning.

7. *Cooking*—Bacteria are killed by heat, the composition of the food is changed, and, in some cases, water is removed.

8. *Refrigeration*—Cold retards bacterial multiplication.

9. *Chemicals*—Benzoic acid is the only one permitted by law. The amount must be stated on the label.

True-False Test

Place the word "true" or "false" before each statement.

- 1. The bacterial content of milk is relatively high.
- 2. A single high bacteria count signifies that the milk is of poor quality.
- 3. If the milk is cooled to 10° C. or lower as soon as milked, no great increase in the number of bacteria will occur.
- 4. A "carrier" working in a dairy may cause milk-borne epidemics.
- 5. Regardless of the degree of temperature to which the milk is heated during pasteurization the time of exposure is twenty minutes.
- 6. Pasteurization completely sterilizes the milk; therefore, further precautions are not needed.
- 7. Food poisoning may be bacterial or nonbacterial in origin.
- 8. Grading of milk is based on the sanitation of the dairy, the health of the cows, methods of handling the milk, the chemical composition of the milk, and its bacterial content.
- 9. Ptomaines play an important part in food poisoning.

Completion Test

- 1. Organisms most commonly found in milk are -----, -----, and -----.
- 2. Bacteria in milk may be classified as ----- and -----.
- 3. The diseases most often spread by milk are -----, -----, -----, -----, and -----.
- 4. Pasteurized milk is milk that has been heated for a short time to a temperature high enough to kill all ----- bacteria.
- 5. The Commission of Milk Standards of New York Milk Committee recommends that milk be heated to a temperature of from ----° F. (----° C.) to ----° F. (----° C.)

References

- Rosenau, M. J.: Preventive Medicine and Hygiene, New York, 1935, D. Appleton-Century Co.
- Boyd, Mark F.: Preventive Medicine, Philadelphia, 1945, W. B. Saunders Co.
- Smillie, Wilson G.: Preventive Medicine and Public Health, New York, 1946, The Macmillan Company.
- Eckles, Combs, and Macy: Milk and Milk Products, New York, 1943, McGraw-Hill Book Co.

SECTION IV

SPECIAL BACTERIOLOGY

CHAPTER XXII

THE COLON-TYPHOID GROUP OF ORGANISMS

Within the colon-typhoid group of organisms are included several related species of bacteria that are characterized by being short gram-negative rods with many similar characteristics. Among them are nonpathogenic bacteria that normally inhabit the intestinal canal and highly pathogenic bacteria that invade the canal and produce disease. The highly pathogenic typhoid bacillus is at one end of the group and the colon bacilli, which are normal inhabitants of the intestinal canal, are at the other end. Intermediate members are the paratyphoid bacilli, the dysentery bacilli, and *B. enteritidis* of Gärtner. A number of other organisms belong to this group, but the ones mentioned are the ones of importance to man. The most important members of this group are capable of bringing about the production of agglutinins in natural infections or when artificially introduced into the body.

I. The Bacillus of Typhoid Fever

Morphological, Staining, and Cultural Characteristics.—*Eberthella typhosa** is a short, motile, gram-negative bacillus that grows luxuriantly on all ordinary media. It does not form spores and does not have a capsule. Typhoid bacilli

The student should familiarize himself with the normal intestinal flora. The child is born with a sterile intestinal tract, but, before or with the first feeding, bacteria are introduced into the tract. If the child is breast-fed, the predominating organism is *Lactobacillus bifidus* (one of the Lactobacilli, a genus of bacteria capable of converting carbohydrates into lactic acid). If the child is bottle-fed, *Lactobacillus acidophilus* occurs in place of *Lactobacillus bifidus*. In addition, a number of other kinds of bacteria are present. In the adult, 30 to 50 per cent of the weight of the feces is made up of bacteria. Because of its acid content, the normal stomach contains few bacteria. If the acid content of the stomach decreases (as often occurs in gastric cancer), the bacterial content of the stomach increases.

*Also known as *Bacterium typhosum*.

grow best under aerobic conditions but may grow anaerobically. The range of temperature at which they grow is from 12° to 40° C. The optimum is 37.5° C. They are capable of remaining alive outside the body for a considerable period. For instance, they live about a week in sewage-polluted water and not only live but multiply in milk. They ferment glucose with the production of acid but not gas. The typhoid bacillus was discovered by Eberth in 1880.

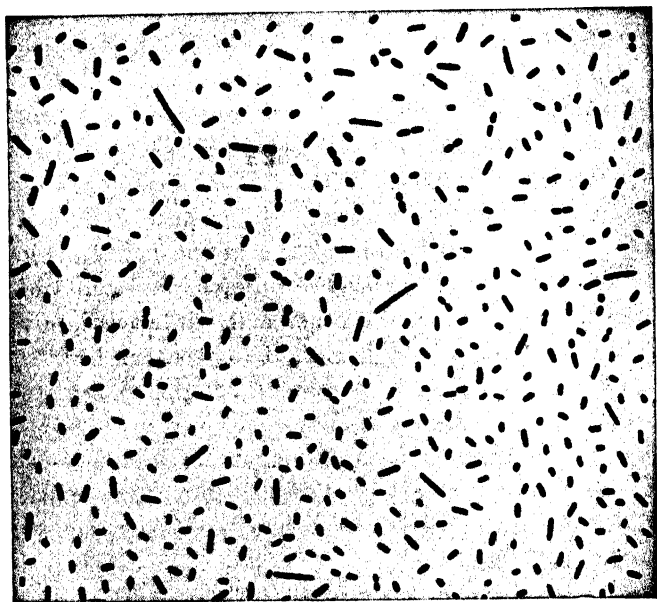


Fig. 75.—Typhoid bacilli. (From Ford: *Textbook of Bacteriology*. W. B. Saunders Co.)

Pathogenicity.—Natural typhoid infections do not occur in any animal other than man. The action of typhoid bacilli is due to endotoxins.

How Typhoid Bacilli Enter the Body.—Every person that contracts typhoid fever does so by swallowing typhoid bacilli which were originally excreted in the feces or urine of a carrier or a person ill of the disease. If the bacilli enter the body by any route other than the alimentary tract, infection will not occur. The incubation period is from seven to fourteen days.

Distribution of Bacilli in the Body.—When typhoid bacilli are swallowed, they penetrate the intestinal lining and attack the lymphoid tissue in the intestinal wall. Peyer's patches bear the brunt of the attack. From the intestinal wall the bacilli pass to the mesenteric lymph nodes draining the area. They multiply in the nodes and pass to the thoracic duct, by which they are delivered to the blood stream. In the blood stream many of the bacilli undergo bacteriolysis with liberation of endotoxins. This brings about the symptoms of the disease. The bacilli that escape bacteriolysis have a tendency to localize in the gall bladder, bone marrow, and spleen. During the first week of illness the bacilli can be found in the blood in more than 80 per cent of cases. After this time they have a tendency to disappear from the blood and are seldom found there in the latter days of the disease. The "rose spots" that are seen on the skin during the early days of illness contain many bacilli. As the disease progresses the bacilli have a tendency to confine their activities to the intestinal wall. They are sometimes found in the feces in the early days but are found more often after the second week of illness, because at this time many bacilli are being thrown into the intestinal canal from the ulcerating Peyer's patches. From 25 to 50 per cent of patients show typhoid bacilli in their urine at some time during the attack, most often after the second week. About 5 per cent of patients become convalescent carriers and about 2 per cent become permanent carriers. Typhoid carriers are of two types: fecal and urinary. In fecal carriers the bacilli multiply in the gallbladder and are excreted in the feces. Infection of the gallbladder with stagnation of bile may aid in the formation of gallstones. In urinary carriers they multiply in the kidney pelvis and are excreted in the urine. Fecal carriers are more common than urinary carriers. Women become carriers more often than men.

How Typhoid Bacilli Leave the Body.—As indicated in the preceding paragraphs typhoid bacilli leave the body by the feces and urine.

How Typhoid Fever Is Spread.—Whatever the mode of transfer, the fundamental basis of every typhoid infection

is the same; i.e., typhoid bacilli from the feces or urine of a carrier of the bacilli or a person ill of typhoid fever reach the mouth of the victim. In some cases the medium of transfer is such that the bacilli multiply en route, but as a rule multiplication does not occur. Media of transfer that promote multiplication are milk and certain foods.

The fingers of those attending a patient with typhoid fever may convey the bacilli to their own mouths or to food which becomes a source of infection. Flies often spread the bacilli to food, etc. Water contaminated with the discharges of a typhoid patient is an important source of infection in rural communities. With improvements in sanitation the widespread epidemics of typhoid fever due to contamination of water supplies with sewage, that once were so common in large cities, have become almost unknown. Milk-borne typhoid epidemics are now more common than water-borne ones. Such epidemics are usually due to a mild case of typhoid fever or a carrier among the personnel of the dairy. Until strict laws regulating the cultivation of oysters and other shellfish were enacted, these were often polluted with sewage-laden water and when eaten raw frequently conveyed typhoid fever. The most important single factor in the spread of typhoid fever is the carrier, especially the carrier who prepares foods that are served raw. There is no successful method of preventing a patient from becoming a carrier or treating him if he does become one. Carriers contaminate their fingers with their discharges and then contaminate food with their fingers. With the advent of modern sanitation typhoid fever has practically disappeared from our larger cities, but unfortunately it is yet rather common in rural communities.

Antibody Formation.—After a typhoid infection has persisted for a week or ten days, agglutinins against typhoid bacilli appear in the blood. They increase during the second and third week of the disease and may persist for weeks, months, or years after the patient recovers. Agglutinins appear in the blood after typhoid vaccination and are usually found in the blood of carriers. The Widal test, which has for its purpose the detection of these agglutinins, is per-

formed by making serial dilutions of the blood serum and mixing them with a suspension of typhoid bacilli. If agglutinins against the bacilli are present, the bacilli will form visible clumps and sink to the bottom of the test tube. The higher the dilution of serum that gives agglutination, the greater its agglutinin content. The blood serum of normal persons may agglutinate typhoid bacilli when diluted 40 or 80 times but does not agglutinate them in higher dilutions. There seems to be a definite relation between the appearance of agglutinins in the blood serum and the disappearance of the bacilli from the blood, because as the former develop the latter disappear.

Immunity.—In about 98 per cent of cases an attack of typhoid fever renders the patient immune for the remainder of his life. The production of an artificial immunity by the administration of typhoid vaccine has been one of the most important factors in the prevention of typhoid fever.

Laboratory Diagnosis.—The laboratory offers four procedures that are of value in the diagnosis of typhoid fever; namely, (1) blood cultures, (2) the Widal reaction,* (3) feces cultures, and (4) urine cultures. The first two are of most value in the diagnosis of suspected cases. The others are of most value in the detection of carriers and in determining when a given case ceases to be a source of danger to others. Blood cultures are of greatest value in the early days of the disease. During the first week from 75 to 80 per cent of cases give positive blood cultures. The percentage falls through the second and third week until not more than 10 per cent of positive cultures are obtained during the fourth week. The Widal test is positive in about 15 per cent of cases during the first week, and the incidence of positive results rises until during the third week it is 90 per cent or more. The test may remain positive for months after recovery. It may be positive after vaccination against typhoid fever and may be positive in carriers. A positive test, therefore, may indicate (1) that the patient now has typhoid fever, (2) that he had typhoid fever months or years before, (3) that he has been vac-

*Devised by Fernand Widal, French clinician and bacteriologist.

nated against typhoid fever, or (4) that he is a carrier. A negative test may be obtained in the early days of the disease or in overwhelming infections. The foregoing statements apply to a Widal test that detects "H" agglutinins only. If a parallel test to detect "O" agglutinins is done, more significance will be given the test. Without attempting a discussion of "H" and "O" agglutinins, which was purposely avoided at the proper place for their discussion, we may say that when an animal is immunized with certain actively motile bacilli, of which the typhoid bacillus is an example, two types of agglutinins will be formed. One type acts on the flagella of the bacteria and is known as "H" agglutinins. The other acts on the body of the bacteria and is known as "O" agglutinins. The latter appear earlier in the disease and indicate the presence of an actual infection with typhoid bacilli or *closely related organisms* while the significance of "H" agglutinins is that given above. Typhoid bacilli may be cultivated from the feces in 50 per cent of cases. The highest percentage of positive feces cultures is obtained about the third week. Positive urine cultures are obtained some time during the course of the disease in about 25 per cent of cases. Convalescent carriers excrete the bacilli in their feces or urine during convalescence, and permanent carriers excrete them permanently but intermittently. Let it be remembered that a single negative result with any of the tests enumerated above does not exclude typhoid fever. This is especially true of feces cultures.

The Prevention of Typhoid Fever.—The prevention of typhoid fever falls into two phases—community prevention and personal prevention. By community prevention is meant those things that can be done by the community as a whole to prevent the spread of disease among its members; by personal prevention is meant those things that can be done to prevent the spread of infection from a person ill of the disease. The most important factors in the community prevention of typhoid fever are (1) a supply of clean pasteurized milk, (2) a pure water supply, (3) the efficient disposal of sewage, (4) the proper sanitary control of foods and eating places, (5) the detection and isolation of carriers, especially

those who handle food, (6) the destruction of flies, (7) the screening of homes, and (8) general typhoid vaccination. Vaccination against typhoid fever will be further considered in the following pages.

Personal prevention depends on isolation of the patient and isolation of the patient does not mean putting him in a room and shutting the doors, but it means the closure of all the routes by which bacteria may be transmitted to others. A nurse attending a case of typhoid fever should consider every secretion and excretion of the patient to be a living culture of typhoid bacilli and should use every means to prevent infection of herself, members of the patient's family, and people in the community. She should have nothing to do with the preparation of food. The feces of the patient should be mixed with three volumes of milk of lime or 5 per cent carbolic acid. The fecal masses should be well broken up to insure thorough penetration, and the mixture should be allowed to stand several hours before discarding. Urine should be mixed with an equal volume of 5 per cent carbolic acid solution or 1:1,000 bichloride of mercury solution. This mixture should be allowed to stand at least two hours. The sputum should be received on cloths and burned. Dishes should be boiled. Linen and bedclothes should be sterilized. Food remains should be burned. The patient's bath water should be sterilized by adding one-half pound of chlorinated lime to 50 gallons of water. The room should be screened, and flies that accidentally gain access to the room should be killed. The hands of the nurse should be disinfected after each contact with the patient or anything that either the patient or his secretions has touched. Disinfection should continue through convalescence, and no patient should be discharged as cured until repeated cultures of feces and urine have failed to show typhoid bacilli.

That the procedures outlined above together with vaccination have materially reduced the incidence of typhoid fever is proved by the following facts. In 1900 the United States death rate from typhoid fever was 35.9 per 100,000 persons; in 1933 it was 3.5 per 100,000. If the incidence of typhoid fever in our army during World War I had been

as high as it was during the Civil War, and the death rate had been as high as it was during the Spanish-American War, there would have been 143,052 cases with 65,313 deaths instead of 1,529 cases with 227 deaths. A review of the typhoid situation in ninety-three of the leading American cities for the year 1946 shows a continued reduction in the disease. In sixty of these cities there was not a single death from typhoid fever. The death rate for these cities as a whole was about 0.15 per 100,000.

Vaccination to Prevent Typhoid Fever.—One of the most potent factors in the control of typhoid fever is the production of an active immunity by the administration of typhoid vaccine which is a suspension in normal salt solution of typhoid bacilli killed by heating to 60° C. for one hour. This vaccine was first used by Sir A. E. Wright of the British Army in 1896 and was introduced into the British Army on a considerable scale in 1898. The vaccine most widely used at the present time is a "triple" vaccine containing *Bact. typhosum*, *B. paratyphosus*, "A," and *B. paratyphosus* "B." Each cubic centimeter contains 1,000,000,000 *Bact. typhosum* and 500,000,000 each of *B. paratyphosus* "A" and *B. paratyphosus* "B." Three injections are given at weekly intervals. The first dose is one-half cubic centimeter, and the second and third doses are one cubic centimeter each. The immunity lasts from one to three years and in some cases longer. Immunity is kept up by revaccination. Formerly this was done by repeating the whole course of injections. Recent work indicates that immunity may be just as effectively maintained, after it has once been established by a series of three injections, by administering a single dose of 1.0 c.c. of vaccine subcutaneously or 0.1 c.c. intracutaneously. Kolmer suggests that revaccination be conducted every two to four years and that it be done by administering intracutaneously 0.1 c.c. triple vaccine.

That universal vaccination alone will materially reduce typhoid fever is proved by the experience of the U. S. Navy during the years 1911, 1912, and 1913, a period in which no revolutionary sanitary developments took place. In 1911 there were 361.57 cases of typhoid fever per 100,000 men.

In 1912 universal vaccination of the naval personnel was put in effect. In 1913 the rate had fallen to 34.89 per 100,000, a reduction of more than 90 per cent! However, the brilliant results obtained by vaccination against typhoid fever should not in the least encourage us to neglect other preventive measures.

II. The Paratyphoid Bacilli (A and B)*

These are two organisms closely related to the typhoid bacillus from the standpoint of morphology, staining reactions, and most of their cultural characteristics. They can be differentiated from *B. typhosus* and from each other by fermentation reactions and agglutination tests. They produce three types of disease: (1) a disease resembling typhoid fever but milder in its manifestations and shorter in its duration, (2) a septic condition resembling one brought about by the pyogenic cocci, and (3) food poisoning.

These organisms are known as *B. paratyphosus* "A" and *B. paratyphosus* "B." *B. paratyphosus* "A" resembles *Bact. typhosum* more closely than does *B. paratyphosus* "B," but infections with the latter are more common. The mode of infection, exit of organisms from the body, laboratory diagnosis, nursing precautions, and prevention in paratyphoid infections are the same as those in typhoid infections. The exact degree of immunity produced by a paratyphoid infection is not known. More recently *B. paratyphosus* "C" has been described. Little is known of its epidemiology.

III. The Colon Bacilli†

There are several different groups of colon bacilli which have certain characteristics in common. They are gram-negative, short motile rods which do not form spores. They grow at a temperature of from 20° to 40° C., but best at 37.5° C. A hemolytic form that is said to be especially pathogenic has been described. They are normal inhabitants of the intestinal canal of man and animals, but under cer-

*The paratyphoid bacilli are known also as the *Salmonella* group after Daniel Elmer Salmon, American veterinary pathologist.

†The colon bacilli are known also as *Escherichia coli*.

tain conditions may escape from the intestinal canal and produce disease. As normal inhabitants of the intestinal canal they aid in the splitting of carbohydrates and combat the implantation of putrefactive bacteria. The presence of colon bacilli in a water supply indicates that it is polluted with fecal matter.

Colon bacilli do not pass through the intestinal wall to produce disease unless one of the following conditions supervenes: (1) the intestinal wall becomes diseased, (2) the resistance of the host becomes lowered, or (3) the virulence of the organism becomes increased. When one of these exists, colon bacilli may pass to the peritoneum or enter the blood. Once outside the intestinal canal and in the tissues of the body, they undergo a remarkable increase in virulence. Among the diseases that colon bacilli may cause are pyelitis, cystitis, cholecystitis, abscesses, and peritonitis. It was formerly thought that peritonitis following intestinal perforation was due to colon bacilli alone, but it is now known that other organisms, such as streptococci and staphylococci, play a part in its causation. From a focus of inflammation colon bacilli may enter the blood stream and produce a septicemia. Vaccines have been used in treating colon bacillus infections, but the results have been variable.

IV. The Dysentery Bacilli*

There are two types of dysentery. One is due to an ameba, a species of protozoon, and is known as amebic dysentery. The other is known as bacillary or epidemic dysentery and is due to *B. dysenteriae*. It is with the latter type that we will deal at this time. Bacillary dysentery may be epidemic or endemic and is usually acute but may be chronic. It is one of the important types of summer diarrhea of infants.

Bacillary dysentery is due to *B. dysenteriae* of which there are two main types: *B. dysenteriae Shiga*, isolated by Shiga in the Japanese epidemic of 1898, and *B. dysenteriae Flexner*, isolated in the Philippine Islands in 1900. Numerous other

*Also known as the Shigella.

closely related types have been found. Dysentery due to the Shiga type of bacillus is much more severe than that due to the other types. That is because this bacillus produces a powerful exotoxin in addition to its endotoxins. The exotoxin acts on the nervous system with the production of paralysis and the endotoxin acts as an irritant on the intestinal canal. Flexner's bacillus does not produce an exotoxin.

The dysentery bacilli are gram-negative, nonspore-bearing rods that grow on all ordinary media at a temperature of from 10° to 42° C.—best at 37° C. They are aerobic and facultative anaerobic. They differ from the other members of the typhoid-colon group in that they are nonmotile.

Pathogenicity.—Dysentery is a human disease and natural infections of the lower animals do not occur.

Mode of Infection.—The mode of infection is practically the same as that of typhoid fever; i.e., the bacilli enter the body by way of the mouth and are transferred from the feces of carriers or patients to the mouth of the victim by food, water, contaminated fingers, or other objects. It seems that contact with persons who have symptomless infections is more important in the spread of bacillary dysentery than food, milk, etc. Flies are an important factor in its spread. Unlike typhoid bacilli, dysentery bacilli are seldom if ever excreted in the urine. The incubation period of bacillary dysentery is forty-eight hours or less.

Distribution of Bacilli in the Body.—Epidemic dysentery is primarily an intestinal infection. The organisms do not invade the blood stream and are seldom if ever found in the internal organs or urine. They are excreted in the feces.

Laboratory Diagnosis.—The only practical method of laboratory diagnosis is the cultivation of the organisms from the stools. Unfortunately this can be done only during the first four or five days of the disease.

Immunity.—An attack of dysentery probably confers some degree of immunity but the same person has been known to have two attacks in a single season.

Prevention.—Bacillary dysentery may be held in check by the sanitary measures that hold typhoid fever in check,

but since there is no satisfactory method of vaccinating against the disease, it remains ready to rise in epidemic form when people are crowded together under sanitary conditions that are not the best. In cases of bacillary dysentery the feces and all contaminated material should be handled exactly as in a case of typhoid fever. Food or milk should not be sold from the premises on which bacillary dysentery is present and those attending the patient should not handle food for others. The patient should not be dismissed as cured until repeated feces cultures have failed to show *B. dysenteriae*. After the patient has recovered, the room should be thoroughly cleaned.

Vaccine and Serum Therapy.—Dysentery vaccines are so highly toxic and variable in their action that they are not often used. Therapeutic serums give fairly good results.

The Summer Diarrheas of Infants.—These diarrheas may be due to many types of infection. Among the organisms that may produce them are dysentery bacilli, saprophytic bacteria of milk, and numerous other bacteria. Summer diarrhea is especially prevalent among bottle-fed babies who are raised in unhygienic surroundings. It is one of the most important causes of infant death. Its prevention depends on breast feeding if this is possible, and if it is not possible the feeding of boiled milk from sterile bottles with sterile nipples.

Questions for Review

1. What does a positive Widal test indicate?
2. Of what value is a single negative result with any of the diagnostic tests for typhoid fever?
3. Discuss the prevention of typhoid fever.
4. Discuss typhoid vaccine as a means of controlling typhoid fever.
5. Under what conditions are colon bacilli able to invade the body tissues?
6. Following intestinal perforation peritonitis is due to what organism?
7. Which dysentery bacillus causes the most severe type of illness and why?
8. Discuss the prevention of bacillary dysentery.

True-False Test

Place the word "true" or "false" before each statement.

- 1. *Bact. typhosum* is a motile gram-negative organism.

- 2. Typhoid bacilli grow best under anaerobic conditions.
- 3. Typhoid bacilli are capable of remaining alive outside the body for a considerable period.
- 4. Every person who contacts typhoid fever does so by swallowing typhoid bacilli which were originally excreted in the feces or urine of a carrier or a person ill of the disease.
- 5. The "rose spots" that are seen on the skin during the early days of illness contain no typhoid bacilli.
- 6. Typhoid bacilli may infect the gallbladder.
- 7. There is a treatment for the typhoid carrier.
- 8. An attack of typhoid fever renders the patient immune for life.
- 9. Dysentery vaccines give fairly good results.

Completion Test

- 1. Two characteristics of the colon-typhoid group of organisms are -----
and -----.
- 2. The typhoid bacillus is also known as -----
and -----.
- 3. The typhoid bacillus was discovered by ----- in the year -----.
- 4. The incubation period of typhoid fever is from ----- to ----- days.
- 5. The typhoid bacilli attack the ----- tissue of the -----.
- 6. Typhoid bacilli reach the blood stream by way of the -----.
- 7. Blood cultures may be ----- during the ----- week of illness.
- 8. Typhoid bacilli may be found in the feces after the ----- week of illness.
- 9. Typhoid carriers are of two types ----- and -----.
- 10. Typhoid bacilli may be spread by -----
----- and -----.
- 11. An agglutination test for typhoid fever is the ----- test.
- 12. Four laboratory procedures that are of value in the diagnosis of typhoid fever are: (1) -----, (2) -----, (3) -----, and (4) -----.
- 13. Two organisms closely related to the typhoid bacillus from the standpoint of morphology, staining reaction, etc., are ----- and -----.
- 14. Two types of dysentery bacilli are ----- and -----.

References

- Smillie, Wilson G.: Preventive Medicine and Public Health, New York, 1946, The Macmillan Company.
- Rosenau, Milton J.: Preventive Medicine and Hygiene, New York, 1935, D. Appleton-Century Co.
- Cook, S. S.: Efficacy of Typhoid Prophylaxis in the United States Navy, *Am. J. Public Health* 25: 251 (March), 1935.
- Patterson, Robert U.: Efficacy of Typhoid Prophylaxis in the United States Army, *Am. J. Public Health* 25: 258 (March), 1935.
- Jordan and Burrows: Textbook of Bacteriology, Philadelphia, 1945, W. B. Saunders Co.
- Typhoid Fever in the Large Cities of the United States in 1946, *J. A. M. A.* 134: 1086 (July 26), 1947.

CHAPTER XXIII

THE ACID-FAST BACTERIA

Nonacid-fast organisms are easily colored with ordinary stains, but the color is quickly removed from them when they are treated with acid alcohol. Acid-fast organisms, on the other hand, are so resistant to the penetration of stains that in order to color them the stain has to be either gently heated or applied over a long period of time. Once colored, however, they are not easily decolorized with acid alcohol. The acid-fast characteristics of bacteria are due to waxy substances contained in their bodies. These bacteria are more closely related to the fungi than any other bacteria. Systematic bacteriology place the acid-fast bacteria in the genus *Mycobacterium*, the members of which are straight or curved acid-fast rods which may show branching or irregular forms. The prefix *Myco* suggests their relation to the fungi.

The acid-fast bacteria of greatest importance to man are *Myco. tuberculosis*, *Myco. leprae*, and *Myco. smegmatis*. The first two are of importance because they are pathogenic. *Myco. smegmatis* does not cause disease, but it is so often an inhabitant of the human body that its differentiation from *Myco. tuberculosis* becomes an important diagnostic problem. In addition to the acid-fast organisms mentioned above, forty or more species exist. Most of them are nonpathogenic, but they may gain access to milk, butter, etc., and be mistaken for *Myco. tuberculosis*. Two are pathogenic for lower animals. One causes rat leprosy and the other causes a granulomatous disease of the intestines of cattle known as Johne's disease. Aside from *Myco. tuberculosis* and *Myco. leprae* none of the acid-fast organisms is pathogenic for man, and with the exception of *Myco. smegmatis* they are seldom found associated with the human body.

I. *Mycobacterium Tuberculosis*

Importance and Distribution.—*Myco. tuberculosis*,* or the tubercle bacillus as it is known in common parlance, is the

*Also known as Koch's bacillus.

causative organism of tuberculosis, which attacks all races of men and many species of lower animals. Tuberculosis is a common disease, but it has dropped from first place as a cause of death in 1900, to the seventh at the present time. Its infectious nature was suspected five centuries before the tubercle bacillus was discovered by Koch in 1882 and it had been produced by artificial inoculation forty years before that time.

The tubercle bacillus is a ubiquitous germ. It is found in the excreta of those that have the disease, in the milk of tuberculous cows, in the rooms that have been occupied by persons with tuberculosis, and in dust that has been contaminated by material containing the bacillus.

General Characteristics of *Mycobacterium Tuberculosis*.—*Myco. tuberculosis* is a slender, rod-shaped, nonmotile, non-spore-forming bacillus. The components of the bacterial cell that render tubercle bacilli acid-fast also render them more resistant than other nonspore-forming organisms to such deleterious influences as drying, germicides, etc. They will remain alive in dried sputum or dust in a dark place for weeks or months and in moist sputum for six weeks or more. Direct sunlight destroys them in one or two hours. Being sufficiently susceptible to heat, however, they are destroyed by the temperature of pasteurization. Five per cent carbolic acid kills *Myco. tuberculosis* in sputum in five or six hours.

Myco. tuberculosis grows with any degree of certainty only on special media. Even then growth is very slow, two to three weeks often elapsing before any growth is visible, whereas ordinary bacteria usually show a visible growth within twenty-four to forty-eight hours. The human tubercle bacillus grows more luxuriantly than the bovine. It grows best at body temperature but may grow at a temperature as low as 29° C. or as high as 42° C. For the best growth of *Myco. tuberculosis* a plentiful supply of oxygen is necessary. The presence of glycerin in the culture medium accelerates the growth of the human bacillus. The bovine bacillus is not affected.

In acid-fast stained preparations tubercle bacilli appear as distinct red rods. They are often beaded in appearance. They are more resistant to decolorization than other acid-fast bacilli.

Types of Tubercle Bacilli.—There are four types of tubercle bacilli which resemble each other rather closely but may be differentiated from each other by animal inoculation and cultural procedures. They are the human, bovine (cattle), avian (fowls), and cold-blooded (frogs, turtles, fish, etc.) types. The words in parentheses after each type indicate the animal in which the type is primarily found. Human tuberculosis may be due to either the human or bovine organism and occasionally cattle become infected with the human bacillus. Human infections due to bovine bacilli are most common in young people and usually occur in children under five years of age. The parts of the body most often involved are the lymph nodes of the neck and abdominal cavity. As people grow older they become more resistant to the bovine bacillus and adult infections due to this organism are uncommon. From 10 to 15 per cent of cases of tuberculosis of the bones and joints are due to the bovine bacillus. Bovine bacilli cause pulmonary tuberculosis in cattle but seldom cause it in man. Tuberculosis of the intestine may be caused by either the human or the bovine bacillus. Bovine bacilli are ingested in unpasteurized milk. If the infection is caused by the human bacillus, the bacteria are usually brought there by the swallowing of sputum from a tuberculous lung. Practically all pulmonary infections in adults and most of them in children are due to the human bacillus. People with pulmonary tuberculosis often develop tuberculosis in other parts of the body, for instance in the kidney with extension to other parts of the urinary system. Small children with pulmonary tuberculosis often have a secondary tuberculous meningitis. Avian tubercle bacilli seldom if ever attack man, and the tubercle bacilli of cold-blooded animals never attack him. Taken all together, it may be said that 95 per cent of human infections are caused by the human bacillus.

The bovine bacillus is more pathogenic for ordinary laboratory animals than the human bacillus. One of the differential points between these bacilli is their action when inoculated into rabbits, the bovine bacillus bringing about the death of the animal in from two to five weeks while it takes the human bacillus about six months to produce death and in some cases death does not occur at all. Guinea pigs are very susceptible to both the human and bovine bacillus but are unaffected by the avian and cold-blooded bacillus. Cattle are frequently infected by avian bacilli and in swine avian infections are very common.

Toxic Products of Tubercle Bacilli.—Tubercle bacilli do not produce exotoxins, hemolysins, or other disease-producing agents, as is the case with many other pathogenic bacteria, but poisonous products that are partly responsible for the symptoms of tuberculosis are liberated when the bacilli undergo disintegration.

When tubercle bacilli are grown artificially, the culture medium contains a product or products known as *tuberculin* which is without effect on a nontuberculous animal but produces powerful and characteristic effects when introduced into the body of a tuberculous animal. These effects are brought about by surprisingly small doses, and if the dose is large enough most disastrous results or even death may follow. There are more than fifty methods of preparing tuberculin, and the nature of each tuberculin depends to some extent on its method of preparation. The tuberculin that is best known and which has been most extensively used is Koch's original (or old) tuberculin, often spoken of simply as "O.T." It is prepared by growing tubercle bacilli for six to eight weeks in 5 per cent glycerin broth, evaporating the culture on a water-bath to one-tenth its original volume and filtering through a bacteria-retaining filter. This tuberculin, therefore, is bacteria-free and consists of disintegration products of the bacilli, substances formed by the action of the bacilli on the culture medium, and the concentrated culture medium. The tuberculin now most often used in performing the tuberculin test is known as P.P.D.

(purified protein derivative). It consists chiefly of the active principle of tuberculin without extraneous matter.

When first discovered tuberculin was highly recommended both as a diagnostic agent and as a specific cure for tuberculosis. As a diagnostic agent it has withstood the test of time. As a therapeutic agent it has, to a great extent, failed which may partly be due to the fact that we yet lack the knowledge necessary to select cases properly and correctly apply the remedy.

Sources and Mode of Infection.—The evidence formerly presented by the postmortem table and the tuberculin reaction showed that practically everyone became infected with tubercle bacilli before reaching the age of eighteen years. In the present age of decreased incidence of tuberculosis a number of persons pass through their early years without becoming infected. In the majority of cases the infection is overcome and active tuberculosis does not develop. Some, however, believe that all infections in adult life are due to the activation of infections that have lain dormant since childhood, by influences that lower body resistance. The weight of evidence indicates that this is not true and most cases of adult tuberculosis are due to reinfections of sufficient severity to overcome the existing immunity rather than to the flaring up of a childhood infection.

The sources of infection are the sputum of persons with pulmonary tuberculosis, excretions from other parts of the human body affected by the disease, and the milk of tuberculous cows. The bacilli are very resistant to drying, sunlight, etc., but have no natural existence outside the body and are transmitted from source to destination by some form of direct or indirect contact. Inhalation is probably the most common mode of human infection and is due to the inhalation of droplets thrown off from the mouth of the tuberculous patient or dust containing the partly dried but still living bacilli. The next most common mode is probably the transfer of the bacilli to the mouth by lips, contaminated hands, handkerchiefs, etc. Small children often contract tuberculosis by crawling on the floor, getting their hands contaminated with tuberculous material, and then placing

them in their mouths. Public drinking cups help spread the disease. Unless washed better than they often are, the eating utensils used by a tuberculous patient may be a source of infection. The milk of a tuberculous mother may convey the infection to her nursing child. Infections with bovine bacilli are usually due to ingestion of the nonpasteurized milk of tuberculous cows. In the cow, tuberculosis usually attacks the lungs, but the cow swallows her sputum and the bacilli are excreted in the feces. The udder and flanks of the cow become contaminated with the feces, and from these locations the bacilli are transferred to the milk. In some cases the bacilli are excreted in the milk as it comes from the udder. It is to be noted that this may occur without demonstrable tuberculous lesions in the udder. About 11 per cent of hogs slaughtered for food shows evidence of tuberculosis. Hogs are susceptible to the human, bovine, or avian bacillus.

When inhaled the bacilli may pass directly to the lungs or through the nasopharyngeal lining and then to the lungs via the lymphatic system. When the bacilli are taken into the alimentary tract, they pass through the mucosa of the throat and nasopharynx to the cervical lymph nodes or through the intestinal wall to the mesenteric nodes from whence they are spread to different parts of the body by the blood or lymph. In such cases the intestinal wall may not be infected. The above discussion indicates that practically all infections are acquired by way of the respiratory or digestive tract and that in adults the majority are acquired by the former route while the latter is the common route of infection in very young children.

The avenues by which tubercle bacilli leave the body depend on the part of the body infected. In pulmonary tuberculosis they are cast off in the sputum; also in the feces of young children and those who swallow their sputum. In intestinal tuberculosis they are cast off in the feces and in tuberculosis of the genitourinary system, in the urine. They may be found in discharges from abscesses and lesions of the lymph nodes, bones, and skin.

Spread of Mycobacterium Tuberculosis Within the Body.

—See Pathology, page 513.

Effects of Tubercle Bacilli on the Body.—Infection with tubercle bacilli renders the body hypersensitive to the tubercle bacillus and its products. Upon this hypersensitivity depend the characteristic reactions obtained when tuberculin is injected into the body of those infected which is used as a diagnostic procedure. Moreover, it at least partially protects those already infected from becoming infected again. Other body changes brought about by the tubercle bacillus are discussed in the portion of this book devoted to pathology. (See page 514.) It seems that the symptoms of tuberculosis are due more to the tissue response of the infected animal than to the activity of the tubercle bacillus or its products.

Tuberculous Infection Versus Tuberculous Disease.—Although practically every person at some time in his life becomes infected with tubercle bacilli, comparatively few develop the active disease because in the great majority of cases the defensive forces of the body overcome the bacilli and the tuberculous focus heals spontaneously or is held in check to such an extent that no systemic evidence of disease is produced. Such infections are known as *latent* infections. Even after the active disease has been established, the defensive forces of the body may overcome it and render it inactive. Such cases are known as *arrested* cases. It should be remembered that latent and arrested foci often contain living tubercle bacilli that spring into activity when the resistive forces of the body are weakened.

Immunity.—As we have already learned, man possesses considerable resistance to tuberculosis. He never possesses a complete immunity. The defensive factors that come into play in a given infection depend on whether or not infection has occurred before. If the person has not had a previous infection resistance depends on the ability of the tissues at the site of infection to surround the bacilli and destroy them or form a limiting wall around them. This is a natural resistance. If the person has been infected before and

the focus of infection has not been completely eradicated, even though symptoms of tuberculosis have never occurred, sensitization of the body to tubercle bacilli and their products brought about by the focus protects to some degree against subsequent infections. This resistance is acquired and for this reason incompletely eradicated infections of childhood often protect against infections in adult life. One proof of this fact is that children who have scrofula seldom contract pulmonary tuberculosis in adult life. This also proves that infections with bovine bacilli protect against infections with human bacilli.

Whether a given infection will terminate in the active disease depends on: (1) the number of bacilli received, (2) their virulence, and (3) the resistance of the person receiving the infection. Conditions that lower body resistance to tuberculosis are dissipation, unsanitary living conditions, lack of sunshine and "fresh" air, and such diseases as measles, whooping cough, typhoid fever, and syphilis. As we have already learned a primary infection increases the body resistance to subsequent infections by rendering the body sensitive to the tubercle bacillus and its products.

The incidence of tuberculosis is high in Negroes, averaging in proportion to population eight cases in Negroes to one in the white race. Not only is this true, but when the Negro contracts tuberculosis the average time which he will live is about one-sixth of that of the white man who contracts tuberculosis. The American Indian and Mexicans are very susceptible to tuberculosis. In women, most cases occur in early adulthood. In men, it is most prevalent at about the fiftieth year.

Not so very long ago it was thought that tuberculosis was hereditary and "ran in families" but we now know that tuberculosis "runs in families" because the members of the family contract it from each other on account of their close association. It is true that the children of tuberculous parents are often not overly strong and have, within their body make-up, factors that predispose to tuberculosis, but a child born of tuberculous parents and at once removed to surroundings where it will not come in contact with tubercle

bacilli has a better chance of escaping tuberculosis than one born of healthy parents but raised in contact with tubercle bacilli.

Persons who live in isolated communities and have not received a tuberculous infection in childhood or youth contract the disease more easily when exposed during adult life than those who have lived in closely crowded and highly infected communities, because the latter are afforded some degree of protection by childhood infections. Attempts to produce an artificial immunity have met with little success.

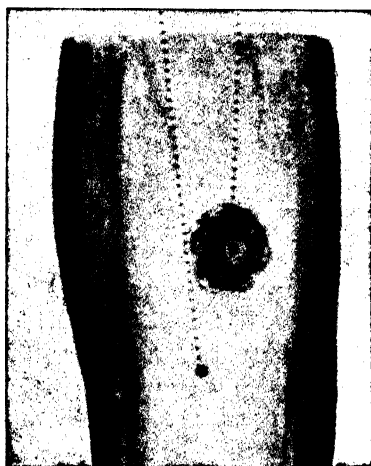


Fig. 76.—Positive tuberculin reaction. The large wheal is the tuberculin reaction and the small dark area is the control test. (From Pottinger: *Clinical Tuberculosis*. The C. V. Mosby Co.)

Laboratory Diagnosis.—Direct microscopic examination of the suspected material after it has been stained with an acid-fast stain is the method most often used in the laboratory diagnosis of tuberculosis. It should be remembered that the failure to find tubercle bacilli in sputum does not rule out pulmonary tuberculosis, because they do not appear in the sputum until the disease is comparatively far advanced. Moreover, they may occur plentifully in one specimen and be scanty or absent in the next. Tubercle bacilli are especially hard to find in urine, cerebrospinal fluid, pleural fluid, joint fluid, pus, etc. Various methods of concentration may

be applied to the material if direct smears fail to reveal the bacilli. Specimens taken from areas where the smegma bacillus is found should be collected in such a manner as to exclude this organism or it will be mistaken for *Mycobacterium tuberculosis*. This is particularly true of specimens of urine.

The best interests of the patient have not been served if we wait to find tubercle bacilli in the sputum before making a diagnosis of pulmonary tuberculosis. The following signs and symptoms are suggestive of, but not positive proof of, incipient pulmonary tuberculosis: (1) repeated colds, (2) loss of appetite, (3) languor and loss of energy, (4) subnormal temperature and rapid pulse, (5) nervousness, (6) afternoon fever, (7) loss of weight, (8) anemia.

Cultural methods are of considerable value in the diagnosis of tuberculosis, but it takes several weeks for tubercle bacilli to develop on culture media and other organisms frequently overgrow them. Special media are required.

When the bacilli cannot be demonstrated in smears made directly from the suspected material or after concentration methods have been applied, they may be frequently demonstrated by animal inoculation. Some of the material is injected subcutaneously in the groin of a guinea pig. If tubercle bacilli are present the pig becomes infected; the tissues about the site of inoculation become thickened and may ulcerate; the inguinal lymph nodes enlarge; the pig gives a positive tuberculin test; a general tuberculosis develops and the animal dies about six weeks after inoculation. As a rule, the pig is not allowed to die but is killed and an autopsy performed when the disease is far advanced.

The *tuberculin test* depends on the fact that persons infected with tubercle bacilli become sensitive to the tubercle bacillus and its products (tuberculin). If a scratch is made on the arm of a person infected with tubercle bacilli and tuberculin is rubbed into the scratch (the von Pirquet test) or some of the diluted tuberculin is injected between the layers of his skin (the Mantoux test), an area of redness and swelling appears at the site of inoculation. If the person is not infected, no reaction will occur. In the "patch"

test a drop of ointment containing tuberculin or a small square of filter paper saturated with tuberculin is placed on the properly cleansed skin and held in place with adhesive tape for 48 hours. A positive test is indicated by redness and papule formation at the site of application. A positive reaction indicates only the presence of an allergic state to tuberculin which may be due to the active disease or lesions that are quiescent. When the limitations of the test are borne in mind and the test is properly applied and correctly interpreted, it becomes a valuable adjunct in the diagnosis of tuberculosis. It was formerly thought that because of the universal prevalence of tuberculosis a positive tuberculin test in persons past early childhood suggested little other than an early infection. This is not quite true at the present time because adulthood may occasionally be reached without infection occurring. In such a person a positive reaction might be indicative of the active disease. Reactions such as the one just described are known as "local" reactions. If tuberculin is given subcutaneously, two other types of reaction may occur. These are the "focal" and the "constitutional." By a focal reaction is meant an acute congestion occurring around a tuberculous focus. This may lead to serious results; for instance, if the tuberculous focus is in the lung, a hemorrhage may occur. By constitutional reaction is meant a sharp rise in temperature and a feeling of malaise lasting for several hours. The tuberculin reaction is of inestimable value in detecting tuberculous cows.

Prevention.—Since tuberculous sputum is the chief source of infection with human bacilli, it should be disposed of in such a manner as to be harmless. It should not be allowed to dry, for then it becomes a source of great danger because it may be blown from place to place and the germs spread over a considerable area. Sputum should be received in containers which have suitable antiseptics in them or on rags or napkins and then burned. Promiscuous spitting should be forbidden. The patient should hold a handkerchief over his mouth when coughing. The two important procedures in the control of the bovine bacillus are the eradication of tuberculous cows and the universal use of pasteurized milk.

The tuberculous patient should have an abundance of rest, fresh air, and sunlight. A tuberculous mother should not nurse her child. The woodwork of a room that has been occupied by a tuberculous patient should be washed with soap and water, followed by bichloride solution or some other suitable antiseptic.

In communities with the best type of health supervision there has been a decided decrease in the incidence of tuberculosis. The mortality from tuberculosis at the present time is about one-fifth as great as it was fifty years ago. This decrease is due to several factors, among which are better living conditions and medical prophylaxis.



Fig. 77.—Applying a tuberculin patch test. The test may be applied to the sternal region of the chest, the abdomen, arm, thigh or back. After the patch has remained in situ for forty-eight hours it is removed and the reaction is read. At the end of another forty-eight hours a second reading is made. At this time the irritation of the adhesive has subsided and the reaction is better developed.

Specific Therapy.—When tuberculin was first discovered, it was widely used as a specific agent for the cure of tuberculosis, but in many instances the cases were improperly selected and the tuberculin was wrongly used. Naturally,

disastrous results followed and tuberculin quickly fell into disuse as a therapeutic agent. At the present time it has gained back a little of its lost prestige, but the kinds of cases in which it can be used are restricted. It does seem to be of distinct value in tuberculosis of the skin. A vaccine (Bacille Calmette-Guérin or B. C. G. vaccine) made from a strain of bovine bacilli that have been cultivated on artificial media so long that they are supposed to have completely lost their virulence for man has been extensively used in European countries to immunize children. Some workers believe that it has a distinct preventive value and that it should be universally used, while others believe that the vaccine on occasion may within itself produce infection. Its exact value must be determined by further use.

II. *Mycobacterium Leprae*

Leprosy is a chronic disease due to *Myco. leprae* that is characterized by a variety of lesions and is very resistant to treatment. It has affected man from the beginning of history, and descriptions of it occupy a prominent place in the Old Testament and other ancient writings. It is estimated that at the present time there are about 4,000,000 lepers in the world and about 1,000 in the United States.

Myco. Leprae (Hansen's bacillus).—*Myco. leprae* is an acid-fast organism that bears a close resemblance to *Myco. tuberculosis*. It occurs plentifully in many leprous lesions but is not found outside the body of man. Infection of the lower animals has not been accomplished and in none of the attempts to grow the organisms artificially has the evidence been entirely conclusive that the organisms grown were true leprosy bacilli.

Mode of Infection.—The imagination of man has clothed leprosy with many attributes that it does not possess. One is that it is a highly communicable disease. This is not true because man contracts leprosy only by prolonged and intimate contact with the disease and even then he often escapes infection. The exact mode of transfer of the bacilli is not known. They probably enter the body through the mouth and nose. The disease is not hereditary, but the

percentage of infection in children associated with leprous parents is very high (30-40 per cent). The incubation period is not definitely known but is estimated at from three to six years.

Laboratory Diagnosis.—A diagnosis of leprosy is most often made by making scrapings from the nasal septum and staining them for acid-fast bacilli. The bacilli are usually found within the cells and in large numbers close together like a packet of cigars. Bacilli may also be demonstrated by making acid-fast stains of material from lesions of the skin and lymph nodes. The fact that they are most often found in scrapings from the nasal septum is taken as an indication that the bacilli enter the body by the respiratory tract. Leprosy and tubercle bacilli may be differentiated by inoculating a guinea pig because leprosy bacilli do not have any effect on the animal.

Prevention and Control.—Leprosy is best prevented by subsistence on a proper diet and living under proper hygienic conditions. Prolonged and intimate contact with lepers is to be avoided. The one important step in the control of the disease is the isolation and segregation of lepers. The rather recently introduced treatment of leprosy by means of chaulmoogra oil or its derivatives has reduced the mortality from leprosy and has rendered some lepers noninfectious to such an extent that they may be released from segregation on parole.

III. The Smegma Bacillus (*Mycobacterium Smegmatis*)

This acid-fast bacillus has no importance as a disease producer but is of importance because it is a normal inhabitant of the prepuce and vulva and may gain access to urine and be mistaken for *Myco. tuberculosis* unless the specimen is properly collected (see page 128). Before it was found that the smegma bacillus was a normal inhabitant of the genitalia, it was thought by some to be the cause of syphilis because it was frequently found in chancres. Of course we now know that this is a harmless contaminant. Smegma bacilli are sometimes found in feces. They may

be differentiated from tubercle bacilli by special staining methods and by the fact that they do not produce disease when inoculated into guinea pigs.

Questions for Review

1. What are the characteristics of an acid-fast organism?
2. Describe the bacillus of tuberculosis.
3. What is the importance of *Myc. smegmatis*?
4. How would you describe a positive reaction to the tuberculin test?

True-False Test

Place the word "true" or "false" before each statement.

- 1. *Myc. smegmatis* is nonpathogenic.
- 2. Acid-fast bacteria are more closely related to fungi than any other bacteria.
- 3. *Myc. tuberculosis* may live in dried sputum or dust in a dark place for several weeks.
- 4. *Myc. tuberculosis* will grow on any ordinary culture medium.
- 5. The bovine type of *Myc. tuberculosis* may infect human bones and joints.
- 6. Old tuberculin was at first considered a specific cure for tuberculosis.
- 7. Old tuberculin is of no value in diagnosing tuberculosis.
- 8. Practically all tuberculous infections in very young children are acquired through the digestive tract.
- 9. Only a small percentage of the adult population has had a tuberculous infection.
- 10. It is commonly believed by the medical profession that tuberculosis may be inherited.
- 11. *Myc. smegmatis* is a normal inhabitant of the genitalia.
- 12. A negative sputum test is positive evidence that tuberculosis is not present.
- 13. Leprosy is a highly communicable disease.
- 14. The most important factor in the control of leprosy is isolation and segregation of "lepers."

Completion Test

1. The acid-fast bacteria of greatest importance to man are _____, _____, and _____.
2. The bacillus of tuberculosis is also known as _____ or _____ bacillus.
3. Direct sunlight will destroy *Myc. tuberculosis* in from _____ to _____ hours.

4. The types of *Myco. tuberculosis* are: _____, _____, _____, and _____.
5. _____ is probably the most common mode of infection by *Myco. tuberculosis*.
6. The sources of infection with *Myco. tuberculosis* are:
 - a. _____
 - b. _____
 - c. _____
7. Conditions which lower the resistance of the body to *Myco. tuberculosis* are:
 - a. _____
 - b. _____
 - c. _____
 - d. _____
8. What are the most commonly used methods of diagnosing tuberculosis?
 - a. _____
 - b. _____
 - c. _____
 - d. _____
9. What are the chief factors in the prevention of the spread of tuberculosis?
 - a. _____
 - b. _____
 - c. _____
 - d. _____
10. *Myco. tuberculosis* was discovered by _____.

References

- Zinsser and Bayne-Jones: Textbook of Bacteriology, New York, 1939, D. Appleton-Century Co.
- Rosenau, Milton J.: Preventive Medicine, New York, 1935, D. Appleton-Century Co.
- Pottenger, F. M.: Tuberculosis, St. Louis, 1948, The C. V. Mosby Co.
- Downes, Jean: How Tuberculosis Spreads in a Rural Community, Am. J. Public Health 26: 31 (Jan.), 1936.
- Topley and Wilson: Principles of Bacteriology and Immunology, Baltimore, 1946, Williams & Wilkins Co.
- Smillie, Wilson G.: Preventive Medicine and Public Health, New York, 1946, The Macmillan Co.

CHAPTER XXIV

BACTERIA PRODUCING EXTRACELLULAR TOXINS

In this chapter we shall consider only those extracellular toxin-producing bacteria that have been known longest and most extensively studied. Others will be considered in subsequent chapters. The toxin production of dysentery bacilli was discussed on page 265.

I. The Bacillus of Diphtheria (*Corynebacterium Diphtheriae*)

Five or six decades ago diphtheria or “membranous croup” as it was then called was one of the major causes of death. Since that time its causative organism has been discovered (Klebs 1883), its epidemiology has become known, diphtheria antitoxin has been discovered (Roux 1894), methods of producing a permanent immunity against the disease have been devised, and the mortality has been reduced from between 30 and 50 per cent to such a level that death seldom occurs in patients that are adequately treated during the early days of the disease.* The causative organism belongs to the genus of bacteria known as *Corynebacterium*, i.e., gram-positive uneven-staining bacteria with clubbed or pointed ends. The word *Coryne* signifies clubbed. *C. diphtheriae* is often called Klebs-Loeffler’s bacillus because it was discovered by Klebs and first grown in a pure culture by Loeffler. The word *diphtheria* is derived from a Greek word meaning leather. It was so named because of the leathery consistency of the diphtheritic membrane.

General Characteristics.—*C. diphtheriae* is characterized by its variation in size, shape, and appearance. It may be straight or curved and may be swollen in the middle or clubbed at one or both ends. When stained it may have a granular, solid, or barred appearance. Rather characteristic is the presence in one or both ends, or scattered throughout

*Within the last few years an especially severe type of diphtheria has appeared in different parts of the world.

the body, of deeply staining granules known as *polar bodies*. *C. diphtheriae* is a gram-positive nonmotile aerobic organism and does not form spores. It grows best at body temperature and on almost all ordinary media but growth is most luxuriant on Loeffler's blood serum. Differential and selective media containing potassium tellurite have been used for cultivating diphtheria bacilli. Some of these media probably give more positive cultures than Loeffler's medium, but the characteristic appearance of the organisms is, to some degree, lost.

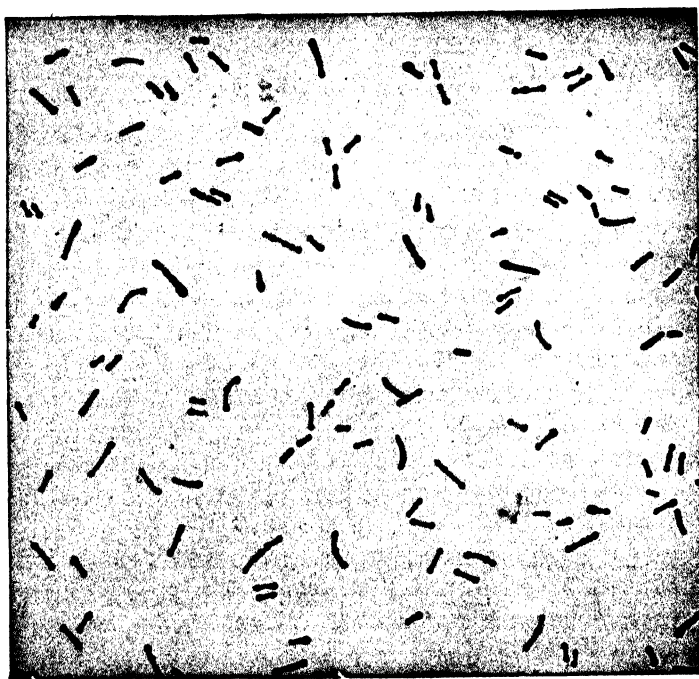


Fig. 78.—Diphtheria bacilli. (From Ford: *Textbook of Bacteriology*. W. B. Saunders Co.)

Diphtheria bacilli are fairly resistant to drying but are easily destroyed by heat and chemical disinfectants. Boiling destroys them in one minute. They may remain alive in bits of diphtheria membrane for several weeks. Like the tubercle bacillus, *C. diphtheriae* is one of the few organisms that may be identified by microscopic appearance alone.

Toxin of *C. Diphtheriae*.—*Diphtheria* bacilli owe their pathogenic action to the extracellular toxin that they produce. The bacilli do not invade the tissues but grow superficially in a rather restricted area, usually on the mucous membrane. The toxin liberated by the bacilli is absorbed into the blood stream where it produces cellular injury, systemic disturbances, and organic degeneration. Its action is directed especially toward certain nerves, the heart muscle, and the kidneys. This explains why paralysis and heart failure occur as late complications in certain cases of diphtheria.

When diphtheria bacilli are grown in a suitable liquid medium, the toxin is thrown off into the medium. After the bacteria are separated from the medium and the toxin in the medium is concentrated, we have the diphtheria toxin of commerce. Such toxins have a toxin content of 200 to 1,000 M.L.D. (see page 213) per cubic centimeter. The toxin has never been separated from the medium in a pure state. It deteriorates with age and is destroyed by a temperature of 60° C.

Not all diphtheria bacilli produce toxin and those that do cannot be differentiated from those that do not by microscopic appearance or cultural characteristics. This is done by injecting a small amount of a liquid culture of the bacilli between the superficial layers of the skin of two guinea pigs, one of which has been given a dose of diphtheria antitoxin. If the bacilli are toxin producers, a zone of inflammation will appear at the site of inoculation in the pig that has not had antitoxin, but none will appear in the pig that has had antitoxin. If they are not toxin producers, neither pig will show a reaction at the site of inoculation. This is known as a "virulence test."

Pathogenicity.—For man and some laboratory animals *C. diphtheriae* is highly pathogenic. In a few cases the pseudomembrane may be so extensive as to produce suffocation unless tracheotomy or intubation is done, but in the majority of cases the serious manifestations of the disease are due to the action of the toxin. The most frequent sites of pseudomembrane formation are the tonsils, pharynx,

larynx, and nasal passages. Less common sites are the vulva, conjunctiva, middle ear, skin, and wounds. The mode of formation and character of the pseudomembrane and the systemic effects of the disease are further discussed in the portion of this book devoted to Pathology (see page 519).

Diphtheria occurs in three common clinical forms: (1) *faucial*, in which the membrane appears on the tonsils and spreads to other parts of the pharynx; (2) *laryngeal*, which is of danger because of its tendency to cause suffocation; and (3) *nasal*, which as a rule does not bring about severe manifestations because the toxin is absorbed with difficulty by the mucosa of the nose. Nasal diphtheria is an important source of infection because it is often overlooked.

Sources and Mode of Infection.—The sources of infection in diphtheria are typical cases, mild undetected cases, and carriers. In ordinary cases the bacteria enter and leave the body by the same route; i.e., by the mouth and nose. The bacilli may be transferred directly from person to person by droplets expelled from the mouth and nose or indirectly by drinking cups, toys, pencils, dishes, etc., which have been contaminated by the buccal or nasal secretions of one harboring the bacilli. The direct method of transfer is the more important. A few milk-borne epidemics have been reported. Such epidemics are usually due to the contamination of the milk with the hand-transferred buccal or nasal discharges of a mild case or carrier among the personnel of the dairy.

Diphtheria Carriers.—In almost one-half of the cases of diphtheria the bacilli leave the body within three days after the disappearance of the membrane, and in four-fifths of cases they disappear within a week, but they sometimes persist for a longer period and the patient becomes a carrier. Also certain persons upon coming in contact with a case of diphtheria or a carrier become carriers without contracting the disease. It has been estimated that from 0.1 to 0.5 per cent of the population are carriers of virulent diphtheria bacilli. The percentage increases during epidemics and in crowded communities during cold weather. Most carriers harbor the bacilli only for a short time

(from a few days to a few weeks), but a few harbor them permanently and remain carriers in spite of most intensive treatment. Virulence tests should be done on the bacilli harbored by suspected carriers because it has been found that a high percentage of the organisms with the morphology and cultural characteristics of diphtheria bacilli that are found in normal throats are not toxin producers and are, therefore, of no danger. Carriers of diphtheria bacilli are immune to diphtheria.

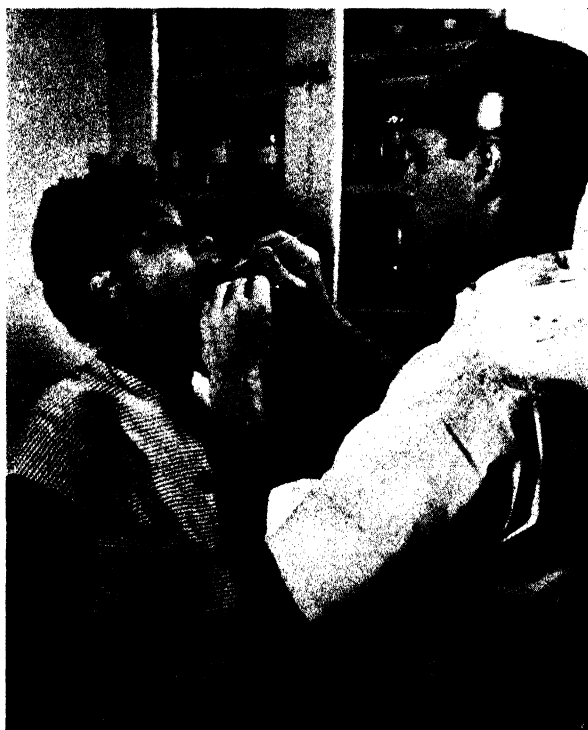


Fig. 79.—Taking a throat culture to detect diphtheria bacilli.

Bacteriological Diagnosis.—The laboratory diagnosis of diphtheria is made by removing some of the material from the membrane with a sterile swab, inoculating a slant of Loeffler's blood serum medium and incubating for twelve to fourteen hours. Smears are then made from the culture

and stained with Loeffler's methylene blue or some of the special stains for diphtheria bacilli. In some cases a diagnosis may be made by finding the bacilli in smears made directly from the membrane, but a failure to find them in no manner indicates that the patient does not have the disease. No antiseptics, gargles, or mouth washes should be used before taking cultures because their use may prevent the proper growth of the bacteria on the medium. Care should be taken to bring the swab in contact only with the site of disease. Cultures should be made from both throat and nose or else a number of cases will be missed.

When a patient presents himself with an ulcerative or membranous inflammation of the throat, both cultures for *C. diphtheriae* and smears for the organisms of Vincent's angina should be made. This is because both conditions are very common and may be easily confused. If only a culture is made, an infection with the organisms of Vincent's angina will be missed because these organisms do not grow in cultures, and many cases of diphtheria will be missed if smears alone are relied upon. Moreover, the two diseases frequently occur together. The finding of diphtheria bacilli in the throat does not always mean that the patient has diphtheria; he may be a carrier. It should be remembered that membranous infections of the throat may be due to causes other than *C. diphtheriae* and that nonmembranous infections with *C. diphtheriae* occasionally occur. It is sound practice to give diphtheria antitoxin in cases showing a clear-cut clinical picture of diphtheria even though laboratory examinations fail to show the bacilli.

Diphtheria Antitoxin.—The general methods of antitoxin production were outlined on page 213. In the immunization of horses for the production of diphtheria antitoxin, toxoid is gradually replacing diphtheria toxin as the immunizing agent. Recent refinements in manufacture have given us a diphtheria antitoxin that contains more than 5,000 units per c.c., and is of less danger from the standpoint of serum reactions than the antitoxins previously manufactured, because in the process of manufacture a very high proportion of the proteins of the horse serum are

removed. Those who give diphtheria antitoxin should remember that it probably is not effective against toxin that has combined with the body cells and that it does not repair injury already done. Therefore, for the best results to be obtained the diagnosis must be made early and sufficient antitoxin must be given at once.

Immunity.—Immunity to diphtheria is due to the presence of diphtheria antitoxin in the blood. Newborn babies receive a passive immunity from their mothers due to the transfer of antitoxin from the maternal to the fetal circulation via the placenta. This immunity is usually lost by the end of the first year. From this time to the sixth year the majority of children are susceptible. Due most likely to minor infections with *C. diphtheriae*, an immunity is re-established during late childhood and youth. About 60 per cent of adults are immune. This figure was once considerably higher, but with the reduction in the incidence of diphtheria and consequent lessening of opportunity to receive minor infections and the institution of vaccination during childhood, which does not give the permanent immunity that repeated minor infections do, there has been a decrease in adult immunity. The presence of from $\frac{1}{500}$ to $\frac{1}{250}$ unit of diphtheria antitoxin per cubic centimeter of blood renders a person immune. Whether or not this amount is present can be determined by the Schick test. An attack of diphtheria renders a person immune for a few weeks or months but not for life. An active immunity to diphtheria may be established by giving toxin-antitoxin or toxoid. Passive immunity is artificially established by giving antitoxin. Most carriers of virulent diphtheria bacilli are immune to diphtheria toxin.

Toxin-Antitoxin.—Toxin-antitoxin is a mixture of diphtheria antitoxin and toxin containing a small excess of the latter used for the purpose of establishing an active immunity against diphtheria. It has all the immunizing powers of the toxin but none of its dangers. Three injections of 1 c.c. each, given at weekly intervals, will bring about a permanent immunity in 75 per cent of cases. It takes so long to establish the immunity, however, that toxin-anti-

toxin affords no protection to those already exposed. To determine whether the use of toxin-antitoxin has brought about a permanent immunity, a Schick test is done six months after the toxin-antitoxin is given. The antitoxin used in the preparation of toxin-antitoxin is made by immunizing goats. This is done in order to avoid sensitizing the recipient of the toxin-antitoxin to horse serum.

Diphtheria Toxoid.—Diphtheria toxoid is diphtheria toxin so modified that it is incapable of causing diphtheria but is capable of bringing about the formation of diphtheria antitoxin when injected into the body. It is prepared by adding from 0.2 to 0.4 per cent formalin to diphtheria toxin and incubating at 37.5° C. until detoxication is complete.

To produce an active immunity toxoid is administered subcutaneously in two or three doses with intervals of three or four weeks between doses. On account of occasional local and general reactions in older children and adults, it is recommended that an intracutaneous test to detect sensitivity to toxoid be done before immunizing persons over six years old. A Schick test should be done three months after toxoid is given.

Alum-precipitated toxoid is prepared by precipitating the toxoid from ordinary toxoid preparations and redissolving. It was formerly thought that a single dose of this concentrated toxoid was sufficient to bring about a lasting immunity, but it is now believed that this is not always strictly true and that much more dependable results may be obtained by giving two doses at intervals of three or four weeks. Even though this is true, we will probably accomplish more in the way of immunizing the general population if we use but a single dose. The precautions to prevent reactions are the same as in ordinary toxoid. A Schick test should be done three months after alum-precipitated toxoid is given.

The Schick Test.—The purpose of the Schick test is to determine whether a person has sufficient diphtheria antitoxin in his blood to render him immune. It is used to detect those who need active immunization and to determine whether active immunization has been effective. The

test is performed by injecting $\frac{1}{50}$ M.L.D. of diphtheria toxin intracutaneously; i.e., between the layers of the skin. If the person's blood contains sufficient antitoxin to protect him against diphtheria, no reaction will occur. If insufficient antitoxin is present, an area of infiltration and redness, from 1 to 2 cm. in diameter, will appear at the site of inoculation within twenty-four to thirty-six hours. It usually persists for four or five days. A control test with heated toxin should be done. A negative Schick test in a child under three years of age does not mean that the child is permanently immune because the result may be due to an immunity received from the mother and which, of course, will finally pass away.

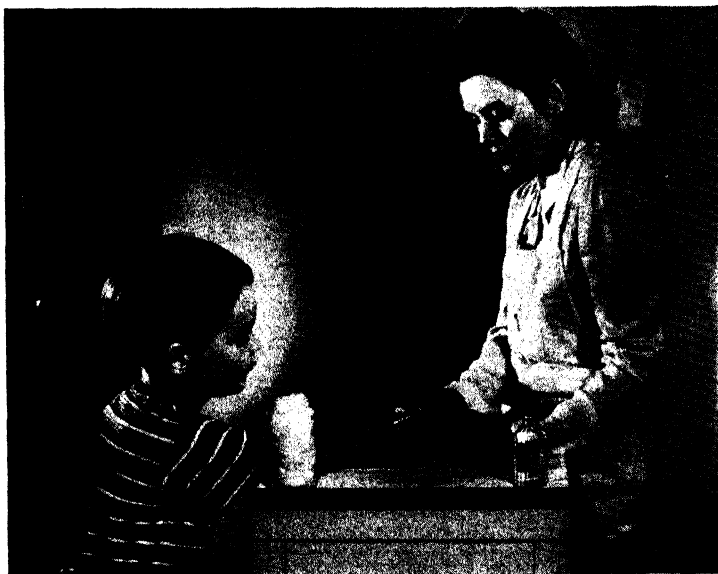


Fig. 80.—Applying the Schick test.

Specific Therapy of Diphtheria.—No therapeutic agent has given more brilliant results than diphtheria antitoxin. By its use much suffering has been prevented and many lives have been saved. To get the best results the disease should be recognized early, and the antitoxin should be given in one large dose. It has been found that after sub-

cutaneous administration the antitoxin content of the blood does not reach its maximum for seventy-two hours. Injections should, therefore, be made intramuscularly or intravenously. It should be remembered that no amount of antitoxin given late in the disease will repair the injury that the toxin has already done. The following schedule of treatment is advised:

1. Mild cases treated on the first day: 5,000 (3,000)* units intramuscularly.

2. Mild cases, second day, and moderate cases first day: 10,000 (5,000) units intramuscularly.

3. Moderate cases second day or later, severe cases first day: from 10,000 to 20,000 (10,000) units intravenously.

4. Severe cases treated the second day or later: from 20,000 to 40,000 (10,000) units intravenously.

In giving diphtheria antitoxin the possibility of a serum reaction should always be kept in mind. This is especially true when the antitoxin is given intravenously.

Diphtheria antitoxin does not affect the diphtheria bacilli themselves, but after it has neutralized the diphtheria toxin in the body, the leucocytes are released from the general fight and they attack the membrane and destroy it with its bacterial content.

Prevention and Control of Diphtheria.—All persons ill of diphtheria should be isolated and neither they nor those who have been in close contact with them should be released until it has been proved that they harbor no virulent diphtheria bacilli in their noses and throats. The mouth secretions and all objects contaminated by them should be disinfected. The eating utensils used by the patient should be boiled. The nurse should be careful that she does not contaminate her hands with the mouth and nose secretions of the patient and then infect herself. Persons known or presumed to be susceptible who are thrown in contact with a case of diphtheria may be temporarily immunized by giving

*The figures in parentheses indicate the dose for a child weighing less than twenty pounds. If, for some reason, diphtheria antitoxin cannot be given intravenously, twice the intravenous dose should be given intramuscularly.

them from 500 to 1,500 units of diphtheria antitoxin. This immunity lasts about 10 days.

The general measures that will cause the greatest reduction in diphtheria are: (1) the detection and isolation of carriers until treatment renders them free of the bacilli, (2) the production of an active immunity in all children under six years of age and all older children and adults, especially physicians and nurses, that show a positive Schick test. A committee reporting to the American Public Health Association in 1935 recommended the following procedures for active immunization against diphtheria: Immunize when possible between the sixth and twelfth months. Give children between six months and six years of age a single dose of alum-precipitated toxoid. If ordinary toxoid is used instead of alum-precipitated toxoid, two doses, with an interval of one or two weeks, are given. Children between six months and six years of age are not given a Schick test either before or after immunizing. In children over six years of age susceptibility is determined by the Schick test and those that are susceptible are given three doses of toxin-antitoxin with intervals of one week between doses. A Schick test is done at the end of six months and a second series of inoculations is given to those showing positive reactions.

The American Academy of Pediatrics in 1940 recommended that the child be immunized against diphtheria by giving toxoid between nine and eighteen months. Tetanus toxoid may be given with the diphtheria toxoid if so desired. A Schick test is done six months later and, if necessary, another attempt at immunization is made. The Schick test is repeated at the sixth year or when an epidemic occurs.

A survey of ninety-three American cities shows that during the last fifteen years the mortality from diphtheria has dropped from 13.13 per 100,000 population to 0.88 per 100,000.

Diphtheroid Bacilli.—This is a group of organisms that bears a close microscopic resemblance to *C. diphtheriae*. They are very numerous and have been isolated from many different sources. They are found in the nose, throat, blad-

der, and prostate. They do not produce toxins and on the whole are nonpathogenic, but under certain conditions some strains may cause a mild chronic inflammation.

II. The Bacillus of Tetanus (*Clostridium Tetani*)

Tetanus or lockjaw is an infectious disease whose manifestations are brought about by the action on the central nervous system of the toxins liberated by *Cl. tetani*. The bacilli have little invasive tendency but remain at the site of infection where they elaborate their powerful toxins. The disease is brought about by the infection of wounds and is not transmitted from person to person.

General Characteristics.—The tetanus bacillus differs from the organisms so far studied in that it forms spores and is anaerobic. Biologically it is a saprophyte and probably never infects wounds that do not contain a small amount of dead tissue.

Cl. tetani stains with the ordinary stains and is gram-positive. The vegetative forms are slightly motile. When sporulation occurs, the spores are situated in one end which gives the bacillus an appearance resembling a roundheaded pin or a drumstick. The sporulating bacillus is not motile. Growth is fairly luxuriant on all ordinary media if anaerobic conditions are maintained. The optimum temperature for growth is 37.5° C. In both cultures and infected wounds the presence of certain aerobic bacteria accelerates the growth of tetanus bacilli. Young cultures contain numerous vegetative bacilli. Old cultures are composed chiefly of sporulating organisms. The bacilli are seldom demonstrated by making cultures from infected wounds. One reason for this is that few bacilli are present.

The vegetative bacilli are no more resistant to destructive influences than other vegetative bacilli. The spores, however, are very resistant. They withstand boiling for several minutes, pass through the intestinal canal unaffected, and when protected from the sunlight remain capable of causing infection for years.

Distribution.—Tetanus spores are common inhabitants of the superficial layers of the soil, especially in certain locali-

ties and always where manure is freely used as a fertilizer. They are normal inhabitants of the intestines of horses, cattle, and other Herbivora. This is why barnyard soils are so frequently contaminated. They are found in the intestinal canal of about 25 per cent of human beings. Vaccines, catgut, and gelatin may sometimes be contaminated. The bacilli have also been found in horsehair and dust. Tetanus is world-wide in distribution.



Fig. 81.—Tetanus bacilli. Note the swollen ends due to spores. (From Park and Williams: *Pathogenic Microorganisms*. Lea and Febiger.)

Toxin Production.—If it were not for the toxin that they produce, infection with tetanus bacilli would be without effect. The toxin which is formed at the site of infection, and when the bacilli are grown on culture media, is one of the most powerful poisons known. This explains why the comparatively few bacilli that are ordinarily at the site of infection are capable of bringing about such profound results. How the toxin travels from the site of infection to the central nervous system is a disputed question. Some observers believe that it passes along the axis-cylinders of the motor nerves. Others believe that it travels along the perineural lymph vessels, and others believe that it is carried there by the blood. In addition to tetanospasmin, the toxin described above, tetanus bacilli elaborate a toxin known as tetanolysin which destroys red blood cells. Tetanus toxin is without effect when taken by the mouth.

Pathogenicity.—When the wide distribution of tetanus bacilli is considered the frequency of infection becomes

rather insignificant. When the disease develops in man, it is highly fatal. Horses often contract the disease.

Source and Mode of Infection.—Tetanus is practically always due to spores that have been introduced into a wound. Whether or not a given wound will be followed by tetanus depends on the type of wound, the chance of becoming contaminated with tetanus spores, and other factors, such as the presence of dead tissue, secondary infection, etc. Punctured wounds are of danger because they provide anaerobic conditions for the growth of the bacilli. Lacerated wounds, gunshot wounds, compound fractures, wounds containing foreign bodies, and infected wounds are of danger because the presence of dead tissue and certain bacteria favors the growth of tetanus bacilli. If such wounds are contaminated by soil, especially heavily manured soil, the chances of infection are greatly increased. All of these things explain why war wounds are so often followed by tetanus. Wounds from blank cartridges are often followed by tetanus. The exact source of infection is not known; apparently it is not due to the wadding of the cartridges as was formerly thought. In many cases the bacilli are probably merely carried from the surface into the tissues. Rusty nail wounds are often followed by tetanus. This is not because the nail is rusty but rusty nails are usually dirty nails and tetanus spores are likely to be in the dirt. Tetanus of the newborn, tetanus neonatorum, is due to infection through the navel. At one time it was a common disease. Puerperal tetanus sometimes occurs in tropical countries. Infection due to bacilli inhabiting the intestinal canal may follow intestinal operations. Although tetanus is more likely to occur under the conditions enumerated above, it may follow trivial wounds inflicted by apparently clean objects. Tetanus spores may be spread over a wide area by flies and high winds.

Tetanus occurs in two clinical forms: acute and chronic. Acute tetanus is characterized by a short incubation period (from three days to two weeks), an abrupt onset, severe symptoms, and a high mortality. Chronic tetanus is

characterized by a longer incubation period (from four to five weeks), less severe symptoms, and a lower mortality. Acute tetanus is more likely to follow wounds about the head and face; i.e., near the brain.

Immunity.—Some persons are more or less immune to tetanus due to the presence of antitoxin in their blood. An active immunity can be produced by the administration of toxoid which closely resembles the similar preparation diphtheria toxoid in its essential nature. Tetanus toxoid is commercially available as plain toxoid or in the alum-precipitated form. When the latter is used, two doses are given at least three months apart. The immunity produced by tetanus toxoid is of short duration and must be stimulated by yearly injections of a single dose. Combined diphtheria and tetanus toxoid, alum-precipitated, gives a high degree of immunity to both diseases.

Prevention and Treatment.—Any wound offering the least suggestion of danger from tetanus should be treated surgically. Punctured wounds should be widely opened and thoroughly cleansed. This serves two purposes: tetanus bacilli and other organisms are removed and the access of oxygen is allowed which is antagonistic to the growth of tetanus bacilli. Lacerated wounds should be thoroughly cleansed and all dead tissue should be removed. The biotherapy to be carried out depends on whether the patient has previously been actively immunized. If he has not been actively immunized, 1,500 units of antitoxin are given, and the dose should be repeated every seven or eight days (taking the necessary precautions to prevent a serum reaction) until the wound is healed. A combined antitoxin against tetanus and the organisms of gas gangrene has been used with good results. If the patient has been actively immunized within the year, he is given 1 c.c. of toxoid for secondary stimulation. If more than a year has elapsed and the patient has not received a secondary stimulating dose, antitoxin must be given as in the case of a person who has not been actively immunized. The Federal Government requires that all serums and vaccines sold in interstate commerce be tested for tetanus bacilli. It has been suggested that persons, such

as soldiers, stockmen, etc., whose occupation exposes them to tetanus be actively immunized with tetanus toxoid. It is practiced on a large scale in the armies of both the United States and England.

Antitoxin is used both intravenously and intraspinally in established cases of tetanus. Although some cases have undoubtedly been benefited by the use of tetanus antitoxin, its therapeutic application as a whole has not been overly encouraging.

III. The Bacilli of Gas Gangrene

Gas gangrene is a highly fatal disease that is due to the contamination of wounds with one alone or any combination of certain anaerobic toxin-producing, spore-forming bacteria. The most important of these are *B. welchii*, *Vibrio septique*, and *B. oedematiens*. All are normal inhabitants of the intestinal canal of man and various animals. Infection is usually brought about by the entrance into wounds of soil that has been contaminated with feces. Lacerated wounds, compound fractures, wounds with extensive death of tissue, and war wounds are especially likely to be sites of gas gangrene. *B. welchii* is found in more than 80 per cent of cases of gas gangrene, but one or both of the other organisms also are usually present. In addition, aerobic pus-producing organisms and certain proteolytic organisms that are without effect on clean wounds but produce marked destruction of tissue in wounds that are infected with gas bacilli are often present.

The organisms responsible for gas gangrene grow in the tissues of the wound, especially the muscle tissue, where they liberate toxins and ferment the muscle sugars with such vigor that the accumulated gas tears the tissue apart and brings about an emphysematous condition of the wound. The toxins elaborated by the bacilli cause edema and necrosis of the wound and enter the blood stream where they cause hemolysis and bring about degenerative conditions of various organs. The bacilli may enter the blood just before death.

Gas gangrene is characterized clinically by local necrosis and edema, the collection of gas in the wound, and a tox-

emia. The patient shows marked pallor and is extremely restless. The systolic blood pressure is markedly lowered. Wound infections are comparatively rare in civil life, but war wounds often become infected. Gas bacillus infections of the abdominal cavity may complicate gangrenous appendicitis, strangulated hernia, and intestinal obstruction. In these cases infection is due to bacilli inhabiting the intestinal canal. The prevention of gas gangrene depends on the proper surgical care of wounds, with the early administration of an antitoxin prepared against the organisms of importance as causes of gas gangrene. This antitoxin has given good therapeutic results. This antitoxin is often combined with tetanus antitoxin. The treatment of the established disease consists of the administration of large quantities of antitoxin, free incision to open the wound as thoroughly as possible, excision of all devitalized tissue, removal of foreign bodies and the establishment of adequate drainage.

IV. The Bacillus of Botulism (*Clostridium Botulinum*)

Botulism is a specific intoxication caused by the ingestion of foods in which *Cl. botulinum* has grown and excreted its toxin. The toxin, not the bacilli, is responsible for the disease. The foods most often responsible for botulism are sausage (from which the disease derives its name), pork, and canned vegetables, such as beans, peas, asparagus, etc. A number of cases have been traced to ripe olives. All of the foods to which outbreaks of botulism have been traced had one characteristic in common: they were prepared by canning, pickling, etc., months or weeks before using. The manner by which the disease is produced may be explained as follows: since the organism is widely distributed in nature, food has ample opportunity of becoming contaminated; when the food is canned or otherwise preserved, the bacilli which are spore formers are not destroyed; during the period between preservation and use the bacilli multiply and produce toxin which is excreted into the food; the food is not heated sufficiently to destroy the toxin when it is prepared for eating, and when ingested the toxin is absorbed through the intestinal wall to produce

its effects. At the present time practically all attacks are due to home-processed foods.

Cl. botulinum is an anaerobic, gram-positive, spore-forming bacillus that is widely distributed in nature and is a normal inhabitant of the intestinal canal of herbivorous animals. It is a common inhabitant of the soil which is the usual source from which foods become contaminated. *Cl. botulinum* is primarily a saprophyte, but infections of laboratory animals have been caused experimentally. Spontaneous infection, however, probably never occurs. The spores resist a moist temperature of 120° C. for four or five minutes.

The toxin of *Cl. botulinum* is one of the most deadly poisons, the mere tasting of food having been known to cause death. It differs from diphtheria and tetanus toxin in that it causes disease when swallowed and is more resistant to heat. It acts on the central nervous system, paralyzing the muscles of deglutition and respiration and bringing about disturbances of vision, dilates blood vessels, and brings about hemorrhage in different parts of the body. It not only attacks man but is also responsible for such diseases of lower animals as fodder disease in horses and limberneck in chickens. The toxin is capable of remaining potent in canned foods for a period of six months or more. It is destroyed by a temperature of 80° C.

There are five types of *Cl. botulinum* from the standpoint of toxin production: A, B, C, D, and E. Type C is divided into two subtypes. Of these types, A and B are most common; C and D do not produce disease in man; and, although of rather common occurrence in Russia, Type E is a very infrequent cause of intoxication in America. Type A is most common in the western portion of the United States; Type B is most common in the central and eastern portions.

A potent antitoxin against *Cl. botulinum* has been prepared. It is of value when given before symptoms have appeared but is of little value after that time. Antitoxin against one type of *Cl. botulinum* is not effective against the toxin of the other types. Therefore, to be therapeutically expedient the antitoxin must be prepared against both the A and B types of bacilli; i.e., the ones that cause disease in man.

Symptoms usually appear within twenty-four hours after the contaminated food is eaten. They consist of general weakness, disturbance of vision (most often double vision), thickness of speech, and difficulty in swallowing. No fever is present and the patient is constipated. Death from cardiac failure or asphyxia usually occurs between the third and seventh day. The mortality ranges from 50 to 100 per cent.

Prevention of botulism depends primarily on: (1) heating to a temperature of 120° C. for more than ten minutes when canning in order to destroy any spores that may be present, (2) cooking canned foods before serving in order to destroy toxins, and (3) proper refrigeration after cooking. If fowls that have been eating discarded food develop limberneck, and the responsible food can be determined, persons known to have eaten the same food should receive botulinus antitoxin. If a case develops among a group of people that have eaten the same food, the other members of the group should be given the antitoxin.

Questions for Review

1. What is the "virulence test" for diphtheria?
2. What is the "Schick test"?
3. What is the difference between diphtheria antitoxin and diphtheria toxoid?
4. Discuss the responsibilities of the nurse as to the prevention and control of diphtheria.
5. Discuss the prevention and treatment of tetanus.
6. Briefly review the important features of gas gangrene.
7. Discuss the toxin of *Cl. botulinum*.
8. How is botulism produced? How may it be prevented?

True-False Test

Place the word "true" or "false" before each statement.

- 1. The diphtheria bacillus was discovered by Loeffler.
- 2. The Klebs-Loeffler bacillus, when deeply stained, shows granules known as polar bodies in one or both ends.
- 3. Like the tubercle bacillus, *C. diphtheriae* may be identified by microscopic appearance alone.
- 4. Diphtheria bacilli deeply invade the tissue and grow.
- 5. Diphtheria may be a milk-borne disease.
- 6. Carriers of diphtheria bacilli are immune to the disease.

- 7. Failure to find diphtheria bacilli in a smear indicates that the patient does not have the disease.
- 8. Newborn babies receive a passive immunity to diphtheria from their mother.
- 9. *Cl. tetani* is gram-negative.
- 10. *Cl. tetani* is a spore-forming organism.
- 11. Tetanus toxin destroys the red blood cells.
- 12. The powerful tetanus toxin acts upon the central nervous system.

Completion Test

- 1. The diphtheriae bacillus is also known as -----
- 2. *C. diphtheriae* is gram-----, and does not form spores.
- 3. Diphtheria bacilli owe their pathogenic action to the ----- toxin that they produce.
- 4. The toxin of diphtheria bacilli is absorbed in ----- where it may affect the -----, -----, and -----.
- 5. In diphtheria, a pseudomembrane may form on -----, -----, and -----.
- 6. In ordinary cases, diphtheria bacilli enter and leave the body by the ----- or -----.
- 7. Two clinical forms of tetanus are ----- and -----.

References

- Zinsser and Bayne-Jones: Textbook of Bacteriology, New York, 1939, D. Appleton-Century Co.
- Rosenau, Milton J.: Preventive Medicine and Hygiene, New York, 1935, D. Appleton-Century Co.
- Recommended Procedure for Diphtheria Immunization, J. Am. Public Health Assn. 25: 712 (June), 1935.
- Diphtheria Mortality in Large Cities of the United States in 1946, J. A. M. A. 134: 1540 (Aug. 30), 1947.
- Smillie, Wilson G.: Preventive Medicine and Public Health, New York, 1946, The Macmillan Company.

CHAPTER XXV

THE GRAM-POSITIVE COCCI

The pathogenic cocci are often called the *pyogenic* cocci on account of their ability to cause the formation of pus. The important gram-positive cocci are the pneumococcus, the streptococcus, and the staphylococcus. The gram-negative cocci will be considered in the next chapter.

I. The Diplococcus of Pneumonia (the Pneumococcus)

In order that this chapter may be better understood, it is introduced with a brief review of the diseases included within the term pneumonia. *Pneumonia* is an inflammatory condition of the alveoli (air sacs), bronchioles, and smaller bronchi of the lungs which leads to a filling of these structures with exudate. It occurs in two forms: *lobar pneumonia* in which one or more pulmonary lobes are completely involved and *bronchopneumonia* (or lobular pneumonia) in which the inflammation occurs in small patches scattered throughout the lungs. Lobar pneumonia usually occurs as a primary disease and in about 95 per cent of cases is due to the pneumococcus of which there are 31 types. Bronchopneumonia is more often secondary than primary and may be caused by a variety of organisms.

General Characteristics of the Pneumococcus.—Pneumococci occur typically as lance-shaped diplococci with their broad ends in apposition. Within the animal body or excretions, each pair is enclosed within a capsule. They are non-motile and like other cocci do not form spores. They are gram-positive.

Pneumococci grow equally well in the presence or absence of oxygen. Their optimum temperature is 37.5° C. Growth is feeble or does not occur at all on media that are not rich in nutritive materials. Growth is most abundant on such enriched media as hormone agar and blood agar. On the latter medium the zone of slight hemolysis and green color surrounding the colony is an important diagnostic character-

istic. The power to form capsules is lost when pneumococci are cultivated for a long time on artificial media.

The pneumococcus is not a very hardy organism and has no natural existence outside the animal body. In the finely divided spray thrown off from the nose and mouth pneumococci live about one and one-half hours in the sunlight. In large masses of sputum they live for a month or more in the dark and about two weeks in the sunlight. They are very susceptible to ordinary germicides and are destroyed in ten minutes by a temperature of 52° C. There seems to be a direct relation between capsule development and the resistance of pneumococci.

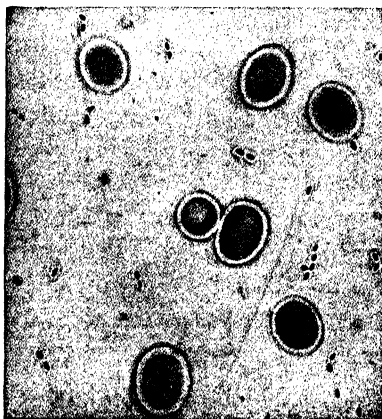


Fig. 82.—Pneumococci. (From McFarland: *Pathogenic Bacteria and Protozoa*. W. B. Saunders Co.)

Types of Pneumococci.—Although all pneumococci are very much alike from the standpoint of microscopic appearance and cultural characteristics, they show distinct differences from the immunological standpoint. This was discovered in 1910 when different cultures of pneumococci were used to immunize animals, and the blood serum of these animals was used to agglutinate the pneumococci with which they were immunized as well as those from various other sources. It was found that the majority of pneumococci fell in one of three rather distinct types (Types 1, 2, and 3) and that an antiserum prepared by immunizing an animal

against pneumococci of one type agglutinated pneumococci of that type only. Pneumococci that did not fall into any of these types were placed in group 4. Later, group 4 was divided into 30 types. It was soon found that some of the types were the same, so that at the present time the pneumococcus types are numbered from 1 to 33, with 26 and 30 omitted. A few years ago therapeutic serums made from rabbits were available for each of these types. These serums have been replaced, to a great extent, by the sulfonamide drugs and penicillin.

Pneumococcus Type 3 differs somewhat from other pneumococci, being characterized by its wide capsule, slimy growth on culture media, and not being lance-shaped. It was formerly known as *streptococcus mucosus*.

The substances that give pneumococci their type characteristics are soluble carbohydrates that occur in the capsules. They can be detected by the precipitin reaction in broth cultures of pneumococci and in the blood and urine of patients with pneumonia.

Toxin Production.—The clinical symptoms of lobar pneumonia indicate that the disease is a toxemia, but a toxin similar to that elaborated by the diphtheria or tetanus bacillus has never been found. They do, however, produce such toxic substances as hemolysins, leucocidins (substances that destroy leucocytes), and necrotizing substances. The last are substances which kill tissue cells.

Pathogenicity.—There seems to be a direct relation between capsule development and the virulence of pneumococci. This may explain why Type 3 infections are accompanied by such a high mortality. A bacteriemia is probably always present in the early days of pneumonia. A persisting bacteriemia is of serious prognostic import. Rabbits and mice are very susceptible to pneumococci. Pigeons and chickens are comparatively resistant.

Mode of Infection, Epidemiology.—Lobar pneumonia is endemic in all centers of population. Epidemics seldom occur but may do so under conditions of exposure and overcrowding, with a concomitant general lowering of resistance. The sources of infection are active cases and carriers, but many

times the connection between case and source of infection cannot be discovered.

Pneumococci enter and leave the body by the same route—the mouth and nose. Infection is usually transferred directly, most often, by droplets from the mouth and nose, but indirect transmission by contaminated objects may occur.

Practically every person becomes a carrier of pneumococci at some time during the year. Those who have been in contact with a case of pneumonia often carry the organisms in their throats for a few days or weeks. Most carriers who have not been in contact with a case of pneumonia harbor comparatively avirulent pneumococci and are of little danger, but Type 3 pneumococci may be found in such carriers. That carriers of Type 3 pneumococci are common while Type 3 infections are comparatively rare is difficult to explain. Most carriers of pneumococci harbor the organisms only for a short time. It was once thought that pneumonia was due to autoinfection; i.e., the patient was infected by pneumococci harbored in his own throat, but it is now known that autoinfection seldom occurs.

Immunity.—Recovery from a pneumococcus infection confers little if any immunity to the disease. Instances have been reported in which a person had pneumonia more than a dozen times. Even if infection with a given type of pneumococcus produces immunity against that type, we would expect pneumonia to recur because there are so many types of pneumococci. The natural resistance of man against the pneumococcus is comparatively high, and a person probably never contracts pneumonia unless his resistance is lowered. Negroes are more susceptible than whites, and men are more susceptible than women. This is probably due to a greater exposure to the conditions that lower resistance.

Laboratory Diagnosis, Determination of Types.—A few years ago, during the era of serum treatment of pneumonia, the laboratory diagnosis of lobar pneumonia consisted not only of detecting the presence in the sputum of the causative organism of the disease, but also of determining the type if it was found to be a pneumococcus. This was because the type of pneumococcus causing the infection had to be known

before a type-specific antiserum could be administered. With the replacement of the serum therapy of pneumonia by the use of penicillin and the sulfonamides, typing is done primarily to determine whether a highly virulent type of pneumococcus is present. Pneumococci may be detected with some degree of certainty by direct microscopic examination of smears stained by Gram's method and for capsules. Confirmatory methods are cultures and the inoculation of white mice. The latter method, which is especially valuable, consists of injecting about 1 c.c. of the emulsified sputum into the peritoneal cavity of a white mouse. The pneumococci outgrow the other organisms, and the mouse becomes ill after five to eight hours, at which time it is killed. The peritoneal cavity will usually contain many pneumococci which can be identified by microscopic, cultural, and typing methods. The inoculation of white mice often shows pneumococci when direct smears fail to do so and always shows them more quickly than cultures.

There are several methods of determining the type of pneumococci. All depend on the action of agglutinating and precipitating serums prepared by immunizing animals against the different types of pneumococci (type serums). The method most often used is the one devised by Neufeld. In this method flecks of sputum or other pneumococcus containing material are mixed with the various type-specific serums. In the mixture in which the type of pneumococcus and serum corresponds, the capsules of the pneumococci will become swollen. The type-specific serums are prepared by immunizing rabbits against the various types of pneumococci. If the sputum contains too few pneumococci or if the typing is otherwise unsatisfactory, some of the sputum may be injected into the peritoneal cavity of a white mouse, as previously described, and in the course of a few hours the typing may be carried out on the pneumococci in the peritoneal exudate.

Differentiation of Pneumococci and Streptococci.—These organisms bear such a close microscopic resemblance to each other that their differentiation is always an important laboratory problem. The important differential points are: (1) the character of colonies on blood agar, (2) in the animal tissues pneumococci have capsules; streptococci seldom have

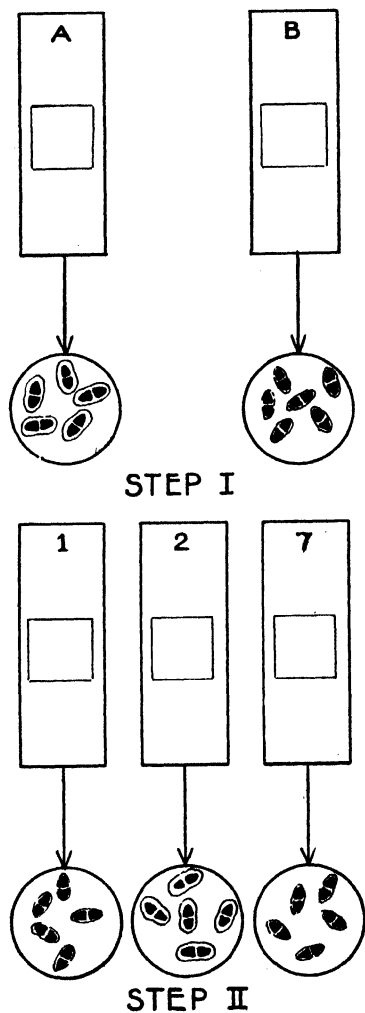


Fig. 83.—Neufeld method of typing pneumococci in sputum. In order to reduce the number of preparations required to type the pneumococci in a specimen of sputum, serums against the thirty-one types of pneumococci are combined into six mixtures with which the sputum is first tested. Later preparations are made with the individual serums in any mixture that shows capsular swelling. The preparations are made by mixing a drop of serum and methylene blue dye with a drop of the well-homogenized sputum and observing the microscopic picture at the end of from fifteen to thirty minutes. In step I preparations with mixtures **A** and **B** are illustrated. The remaining preparations (**C**, **D**, **E**, and **F**) are omitted because of space. It is noted that capsular swelling occurs in mixture **A** but not in **B**. This indicates that the pneumococci belong to Type 1, 2, or 7 because these are the types represented by the serums in mixture **A**. In step 2 preparations with these monovalent serums are illustrated. Capsular swelling indicates that the pneumococci belong to Type 2. A sputum may contain more than one type of pneumococci.

capsules, (3) when one part of bile is added to three parts of a liquid culture pneumococci are dissolved; streptococci are not, (4) pneumococci ferment inulin; streptococci do not, and (5) pneumococci are more pathogenic for mice than are streptococci. Further differential aids are agglutination and precipitation tests with specific antiserums.

Specific Therapy.—Antipneumococcus serum was originally prepared from the horse. It was later prepared from both horses and rabbits. With the advent of the sulfonamide compounds and penicillin, the need for antipneumococcus serum has been greatly reduced, and it is seldom used.

Attempts have been made to establish a permanent immunity to pneumonia by means of vaccines. So far no definite conclusions can be drawn. The results obtained with vaccine made from capsular substances are encouraging.

Prevention.—To prevent pneumonia is a baffling proposition because its epidemiology is not well understood. A person with pneumonia should be isolated and the number of persons coming in contact with him should be restricted. The discharges from the mouth and nose should be burned or disinfected. The hands and all objects, such as spoons, cups, etc., which may be contaminated by the discharges of the patient should be disinfected. The spray leaving the mouth of the patient while talking or coughing should be prevented from coming in contact with others. The patient and attendants should not be released from isolation until their mouths and throats are free of virulent pneumococci. General precautions that prevent pneumonia are the avoidance of crowding, droplet infection, and those conditions that lower body resistance. The use of prophylactic vaccination was discussed in the preceding paragraph.

Other Causes of Lobar Pneumonia.—Of the 5 per cent of cases of lobar pneumonia that are not due to the pneumococcus the majority are due to Friedländer's bacillus, *H. influenzae*, or streptococci.

Other Diseases Caused by Pneumococci.—Other conditions that may be caused by pneumococci are empyema, endocarditis, meningitis, arthritis, otitis media, peritonitis, and

corneal ulcers. Some of these occur as complications of pneumonia and others occur as primary conditions. *Pneumococcus peritonitis* has a tendency to occur in children. *Pneumococcus otitis media* has a marked tendency to spread to the meninges. Before the introduction of the sulfonamide drugs the mortality in pneumococcus meningitis was practically 100 per cent. It has been reduced to about 60 per cent. Corneal ulcers due to pneumococci may become sources of great danger and operations on the eye should be avoided when such ulcers are present.

II. The Streptococci

A. GENERAL CONSIDERATION OF STREPTOCOCCI AND THE DISEASES THEY CAUSE

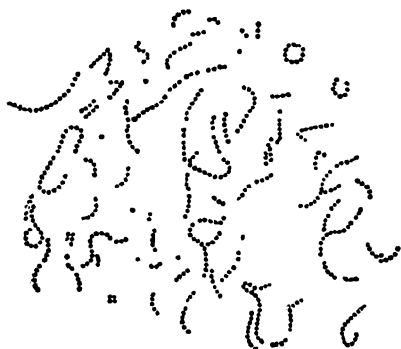
The term "streptococcus" rests on a morphological basis and includes all cocci that occur in chains and are insoluble in bile. The latter differentiates them from pneumococci. Within this group of organisms are found marked variations in cultural characteristics and disease-producing properties. Some produce most deadly diseases; others are without pathogenic effect. As a whole, streptococci are probably responsible for more illness and are capable of causing more different kinds of disease than any other group of organisms. They are capable of attacking any part of the body and are equally capable of causing primary disease or acting as secondary invaders.

General Characteristics.—Typical streptococci occur as cocci of variable size arranged in long or short chains. Long chains may contain 50 or more organisms. Short chains may contain as few as four or six. They may have a tendency to be arranged in pairs within the chains. Streptococci are nonmotile, gram-positive, and do not form spores.

The majority of streptococci grow best in the presence of oxygen but may grow in its absence. A few species are strict anaerobes. They grow well on all fairly rich media and a visible growth usually appears within twenty-four to forty-eight hours. Growth is especially luxuriant on hormone media or media containing unheated blood serum, whole blood, ascitic or pleural fluid. They multiply in milk. Their cultural characteristics on blood agar plates will be discussed

in the paragraphs on classification. Streptococci grow best at body temperature but may grow through a temperature range of from 15° to 45° C. They are not soluble in bile and do not ferment inulin, characteristics that are of importance in differentiating them from pneumococci.

Streptococci may remain alive in sputum or other excreta for several weeks and may live in dried blood or pus for several months. They are destroyed by a temperature of 60° C. in from thirty to sixty minutes. They are killed in fifteen minutes by 1:200 carbolic acid solution, 1:200 bichloride solution, 1:1,000 tincture of iodine, or 2 per cent mercuriochrome.



Katharine Hill

Fig. 84.—Streptococci. (From Webster: *Diagnostic Methods*. P. Blakiston's Son and Co.)

Classification.—Streptococci have been classified on the basis of fermentation of sugars, pathogenicity, or serological behavior. A method that is useful as a basis of identification is their action on blood-agar plates. In carrying out this classification blood-agar plates are prepared by melting nutrient agar, cooling to 45° C., adding sterile defibrinated blood in the proportion of 5 to 10 parts of blood to 100 parts of blood-agar mixture, pouring in Petri dishes, and allowing to cool. The surface of the "plates" is inoculated with the material in which the type of streptococci is to be determined and incubated at 37.5° C. for twenty-four

hours or longer. Depending on their action on the blood in the blood-agar plates, streptococci may be classified into the following groups within which are many different strains:

1. Alpha or viridans type—colony surrounded by a green halo; hemolysis slight or absent.
2. Beta or hemolytic type—colony surrounded by a clear colorless zone of hemolysis.
3. Gamma type—colonies show neither hemolysis nor color change.

As a general rule, the hemolytic type (*Streptococcus hemolyticus*) is the most virulent and is associated with acute fulminating infections, while the viridans type is most often associated with chronic infections. Infections due to the viridans type (*Streptococcus viridans*) (example—subacute bacterial endocarditis) are often just as surely fatal as infections due to hemolytic streptococci. Many, but not all, strains of streptococci of the gamma type are nonpathogenic. It will be noted that the colonies of pneumococci and *Streptococcus viridans* on blood-agar plates are very much alike. Which organisms we are dealing with may be determined by bile solubility and inulin fermentation tests.

By serological (precipitin) methods streptococci may be divided into nine groups, A, B, C, D, E, F, G, H, and K,* which correspond in a general way to their pathological action. These groups may be further subdivided into a large number of types which apparently have a more exact significance from the standpoint of their relation to different kinds of infection. Most human infections are due to group A streptococci, the members of which are hemolytic and are divided into at least forty types. Streptococci pathogenic for the lower animals usually belong to Groups B or C. Streptococci belonging to the remaining groups are usually nonpathogenic.

In the paragraphs that are to follow the text will be directed mainly toward a description of the hemolytic streptococci, and the dissimilar characteristics of the other types will be noted.

Poisons Produced by Streptococci.—Streptococci elaborate certain extracellular poisons some of which can be called

*Classification of Lancefield.

exotoxins. Among these poisons are (1) hemolysins, (2) leucocidin, (3) fibrinolysin, (4) spreading factor, and (5) erythrogenic toxin. *Fibrinolysin* is of importance in that it destroys fibrin which is the component that forms the framework of blood clots. Blood clots play an important part in the healing of wounds and in preventing the spread of local infections. The *spreading factor* is a factor which increases the permeability of the tissues to such substances as bacteria, vaccine virus, toxins, etc. The *erythrogenic toxin* gives a marked erythema when injected into the superficial layers of the skin. It is the scarlet fever toxin of Dick.

Pathogenicity.—Different strains of streptococci vary in their disease-producing capacity from those that are non-pathogenic to those that cause rapidly fatal infections.

Streptococci may be responsible for localized inflammatory reactions, abscesses, or septicemias, the nature of the lesions depending upon the virulence of the streptococci, the number introduced into the body, the mode of introduction, and the resistance of the host. Allergic manifestations may accompany certain streptococcus infections. For instance some cases of arthritis and rheumatism may be allergic reactions to streptococcus infections.

As a rule, the more virulent an infection the more virulent are the streptococci isolated from the lesions for animals of the same species. Usually their virulence is lowered when introduced into animals of another species. Streptococci have a tendency, when transferred from one animal to another, to produce the same type of lesion in the new host as was in the animal from which the infection was received.

Rabbits and white mice are more susceptible to streptococci of human origin than other laboratory animals.

Human Diseases Due to Streptococci.—*Streptococcus hemolyticus* is the most common cause of acute endocarditis, septicemia, and puerperal sepsis. It may cause pneumonia, boils, abscesses, cellulitis, peritonitis, tonsillitis, lymphangitis, infection of surgical wounds, osteomyelitis, empyema, and otitis media. From the middle ear a streptococcus infection may spread to the mastoid cells and cause a mastoiditis. From either the middle ear or the mastoid cells the infection may

spread to the meninges and cause a streptococcus meningitis. Until the advent of the sulfonamide drugs, streptococcus meningitis was fatal in practically 100 per cent of cases. The mortality now is about 25 per cent. Hemolytic streptococci are responsible for the majority of bronchopneumonias, complicating whooping cough, measles, and influenza. Such bronchopneumonias are highly fatal and may reach epidemic proportions when outbreaks of whooping cough, measles, or influenza occur in communities where the incidence of carriers of hemolytic streptococci is high. Hemolytic streptococcus pneumonia often ends the scene in such chronic diseases as tuberculosis and cancer.

Streptococcus viridans is the usual cause of subacute bacterial endocarditis. It also causes such conditions as root abscesses of teeth, infections of the nasal sinuses, etc. It is responsible for many focal infections.

Streptococcus Infections in Lower Animals.—The majority of streptococcus infections in lower animals are due to streptococci belonging to Lancefield's Groups B and C. Spontaneous infections causing lymphadenitis may occur in rabbits and white mice. Strangles, an acute communicable disease of the upper respiratory passages of horses, is due to streptococci. Streptococcus mastitis, a serious disease of cows which renders milk unfit for use, is of common occurrence.

Source and Mode of Infection.—Streptococci are normal inhabitants of the mouth, nose, throat, and respiratory tract; i.e., there are many streptococcus carriers. They may be conveyed from person to person by direct contact or by contaminated objects, hands, and surgical instruments. They usually enter the body by the respiratory tract or through abrasions or wounds of the skin. For streptococci to enter the body by way of the skin only a minute abrasion is necessary, and such abrasions have many times been the cause of fatal septicemias in physicians and nurses. Streptococci leave the body by way of the mouth and nose and in exudates from areas of infection. One type, *Streptococcus faecalis*, which is of slight pathogenicity, is a normal inhabitant of the intestinal canal and is excreted in the feces.

Laboratory Diagnosis.—Streptococci may be detected by smears and cultures from the site of disease. In septicemias due to hemolytic streptococci the organisms can be detected by blood cultures in a high percentage of cases. In such conditions as subacute bacterial endocarditis the organisms escape into the blood intermittently, and repeated cultures may have to be made before they are found.

Immunity.—With the exception of scarlet fever, streptococcus infections are not followed by an immunity to subsequent attacks, and in scarlet fever the immunity is established against scarlet fever toxin, not the organisms themselves. However, the injection of streptococci and their products into suitable animals is followed by antibody formation. Agglutination tests show that there are many serological strains of streptococci capable of producing each disease.

Prevention.—When nursing a patient with a streptococcus infection, the nurse should remember that she is dealing with an infection that may be most virulent and is very easily spread. Physicians and nurses attending such infections should not attend an obstetrical case or surgical operation until they are incapable of spreading the infection. This is especially true in scarlet fever and erysipelas. Obstetrical cases should be handled with strictest aseptic care because the recently emptied uterus is very susceptible to infection. The buccal and nasal secretions from a patient with bronchopneumonia should be handled in the same manner as those from a patient with diphtheria. A case of bronchopneumonia occurring in a ward occupied by patients with influenza or measles should be immediately isolated. No matter how trivial an operation, it should be done with the most painstaking aseptic technic. Conditions favoring contact infection should be avoided and all wounds and abrasions on the body should be thoroughly disinfected.

Specific Therapy.—The following statements apply to streptococcus infections other than scarlet fever and erysipelas. Saline vaccines have been used to produce an active immunity, but their efficacy is doubtful. An antistreptococcus serum has been prepared by immunizing horses with streptococci. It seems to be of some value in treating in-

fections due to hemolytic streptococci but is of no value in infections due to the other types.

B. THE STREPTOCOCCUS OF SCARLET FEVER

Scarlet fever is an acute infection due to toxin-producing hemolytic streptococci belonging to Lancefield's Group A. Only about 10 per cent of streptococci in this group are capable of causing scarlet fever. As is the case in diphtheriae, the bacteria grow locally and the toxin is absorbed into the blood, bringing about the constitutional effects of the disease. The streptococci themselves are responsible for the sore throat and cause the inflammatory complications, such as middle ear infections, etc. There is a rather close relation existing between the hemolytic streptococci causing scarlet fever, erysipelas, and puerperal septicemia.

Source and Mode of Infection.—The sources of infection are the nose and throat secretions of patients or carriers and pus from infected lymph nodes, ears, etc. The organisms are present throughout the course of illness and may persist in the nose and throat, or in the pus from infected ears, etc., for weeks or months thereafter. As long as a person harbors the organisms he is a source of danger to others. The desquamated scales do not transmit the infection.

The organisms usually enter the body by the mouth and nose. Less common avenues of entrance are wounds, burns, and the parturient uterus. Infection may be transmitted by direct contact or by means of contaminated objects, such as handkerchiefs, towels, pencils, toys, dishes, etc. Milk-borne epidemics due to contamination of the milk by the secretions of an unrecognized case or carrier among the personnel of the dairy sometimes occur.

The Toxin of Scarlet Fever Streptococci.—The toxin of scarlet fever streptococci is liberated by the organisms at the site of infection and is absorbed into the body, bringing about the rash and other constitutional effects of the disease. It is prepared artificially by growing scarlet fever streptococci for five days in broth and separating the bacteria from the broth, which contains the toxin, by filtration. Toxin prepared in this manner is capable of causing scarlet fever when given

in large doses, and when injected in very small amounts into the skin of persons susceptible to scarlet fever, it gives rise to an inflammatory reaction. The latter is the basis of the Dick test. It also is capable of bringing about an active immunity and the formation of antitoxin when injected into the animal body. The unit of measurement of scarlet fever toxin is known as the "skin test dose" (S. T. D.) which is the smallest amount of toxin that will cause an inflammatory reaction when injected into the skin of a susceptible person. It is necessary to use susceptible persons for the test because the majority of laboratory animals are not susceptible to scarlet fever toxin. However, a method of testing in which the white goat is the test animal has been devised.

Immunity.—Immunity to scarlet fever is due to scarlet fever antitoxin in the blood. Whether or not a person has sufficient antitoxin to render him immune can be determined by the Dick test. Infants inherit an immunity from their mothers. This is lost within a year and susceptibility increases until the sixth year. After the sixth year susceptibility decreases until adult life, at which time the majority of people are immune. Only about one-third of the people contract scarlet fever when exposed during the age of greatest susceptibility. An attack is usually followed by a permanent immunity. It should be remembered that although an immune person will not be attacked by scarlet fever toxin, the streptococci themselves may invade his body and cause such localized inflammations as tonsillitis, abscesses, otitis media, etc. Immune persons may harbor the organisms for a long time and may spread the infection widely without being recognized.

The Dick Test.—The Dick test is performed by injecting between the layers of the skin of the forearm 0.1 c.c. of scarlet fever toxin so diluted that one S. T. D. is injected. In immune persons the antitoxin in the blood neutralizes the injected toxin and no reaction occurs. In susceptible persons no antitoxin is present, and the toxin attacks the cells around the site of injection, producing, within twenty-four hours, an area of inflammation and redness of the skin at least 1 cm. in diameter. The test is positive at the beginning but becomes negative during the course of an attack of scarlet fever.

The Schultz-Charlton Phenomenon.—If a small amount of the blood serum of a person convalescent from scarlet fever or of an animal that has been immunized against scarlet fever is injected intradermally into an area of scarlet fever rash, the rash blanches at the site of injection. This is due to the neutralization of the toxin in the skin by the injected antitoxin. This test is of value in the differentiation of scarlet fever from measles, German measles, erythema, urticaria, etc.

Antitoxin.—Scarlet fever antitoxin is prepared by immunizing horses with scarlet fever toxin or mixtures of toxin and scarlet fever streptococci. If the toxin-streptococcus mixture is used, the resulting serum is antibacterial as well as antitoxic. A unit of scarlet fever antitoxin is the amount required to neutralize fifty skin test doses of scarlet fever toxin.

Specific Therapy.—Scarlet fever antitoxin combats the toxemia of scarlet fever and decreases the severity of its symptoms. Pure antitoxic serums have no effect on the streptococci themselves but lessen complications. The initial dose for cases of average severity is from 5,000 to 10,000 units intramuscularly. It should be repeated if necessary. Antitoxin may be used to protect those exposed. An active immunity lasting for two years or more may be established by giving 5 or 6 injections of increasing amounts of scarlet fever toxin until a total amount of from 50,000 to 100,000 skin test doses is given. An interval of from seven to ten days should elapse between injections.

Prevention.—The scarlet fever patient should be isolated and the discharges from the mouth and nose as well as all contaminated articles should be disinfected. The disinfecting procedures are the same as those in diphtheria. Those attending a case should exercise every precaution to prevent the spread of infection to others, especially obstetrical or surgical cases. The patient should remain isolated until the discharges from the mouth and nose are free of scarlet fever streptococci and all complicating abscesses, middle ear infections, etc., have healed.

Pasteurization prevents milk-borne epidemics. While active immunization is certainly desirable in some cases, for in-

stance among physicians and nurses who attend scarlet fever cases and in institutions where the probability of infection is high, the low incidence of infection and the mild nature of the disease at the present time render active immunization of the general population less necessary than in highly communicable diseases, such as diphtheria.

C. ERYSIPELAS

Erysipelas is an acute inflammation of the skin which is due to hemolytic streptococci belonging to Lancefield's Group A. The organisms grow at the site of infection and produce toxins that are responsible for the constitutional symptoms. They are not present in the central portion of the inflamed area but are found at the periphery.

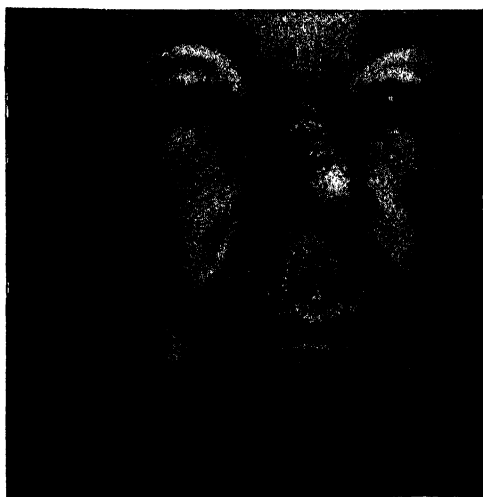


Fig. 85.—Erysipelas of face. Notice the characteristic edema. (From Sutton and Sutton: *An Introduction to Dermatology*. The C. V. Mosby Co.)

Mode of Infection.—The portal of entry of the organisms is most often a wound, fissure, or abrasion. Erysipelas streptococci occur almost exclusively in the lymph channels of the inflamed area and spread peripherally as the disease progresses. When found in the blood an unfavorable prognosis is indicated. Erysipelas may be complicated by abscesses, pericarditis, arthritis, endocarditis, septicemia, and

pneumonia. Ordinary cases without open wounds or superficial discharges will not transmit the infection to others.

Immunity.—Instead of bringing about a condition of immunity an attack of erysipelas seems to render the patient more susceptible to future attacks. An erysipelas antitoxin has been prepared. Some workers state that scarlet fever antitoxin gives good results in the treatment of erysipelas which indicates a close relationship between the streptococci causing the two diseases.

D. RHEUMATIC FEVER

(See Pathology, page 505.)

E. PUERPERAL SEPSIS

Puerperal sepsis is usually due to a hemolytic streptococcus which usually reaches the uterus via contaminated hands, instruments, etc. Most of these streptococci belong to Lancefield's Group A. This disease is responsible for about 40 per cent of the deaths traceable to childbirth. The close relationship existing between the organisms of scarlet fever, erysipelas, and puerperal sepsis, and the nursing precautions based upon this relationship have been indicated in preceding paragraphs.

F. SEPTIC SORE THROAT

Septic sore throat is an ulcerative inflammation of the throat that is accompanied by severe symptoms and a high mortality. It is caused by hemolytic streptococci belonging to Lancefield's Group A. Most cases are caused by drinking milk that has been contaminated with the mouth and nose secretions of a carrier. The carrier may harbor scarlet-fever-producing streptococci or some other type. In some cases the udder of a cow becomes infected through the milk ducts by the discharges of a carrier during milking, and the streptococci may be discharged in the milk for several weeks. However, most cases of streptococcus mastitis in cows are due to a specific streptococcus, *Streptococcus agalactiae*, which belongs to Lancefield's Group C and seldom attacks man. Septic sore throat is not likely to be transmitted directly from person to person.

III. Staphylococci

General Characteristics.—Staphylococci are cocci that occur typically in grapelike clusters. Under special conditions they may occur singly, in pairs, or in short chains. They are gram-positive, nonmotile, and do not form spores. They grow luxuriantly on all culture media. Most grow best in the presence of oxygen but may grow in its absence. A few are strictly anaerobic. They grow best between 25° and 35° C., but may grow at a temperature as low as 8° C. or as high as 48° C. Growth of the aerobic staphylococci is often accompanied by the production of pigment upon which characteristic classification of the staphylococci is based. Some produce hemolysis on blood agar.

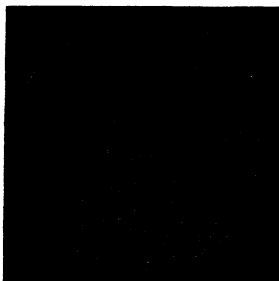


Fig. 86.—*Staphylococcus aureus*. (From Gradwohl: *Clinical Laboratory Methods and Diagnosis*. The C. V. Mosby Co.)

Staphylococci are the most resistant of all nonspore-forming organisms to such destructive influences as heat, drying, and the action of chemicals. They frequently resist a temperature of 60° C. for an hour and may live in dried pus for weeks or months.

Classification.—Based on the color of pigment produced when grown on artificial media, staphylococci are classified as *Staphylococcus aureus*, *Staphylococcus albus*, and *Staphylococcus citreus*. *Staphylococcus aureus* produces a golden yellow pigment; *Staphylococcus albus* produces no pigment, and *Staphylococcus citreus* produces a lemon-colored pigment. According to some observers *Staphylococcus albus* is merely a *Staphylococcus aureus* that has lost its power of pigment production. There are three species of strictly anaerobic

staphylococci. These inhabit the body cavities. As disease producers, the aerobic staphylococci are by far more important than the anaerobic.

Pathogenicity.—Some staphylococci are nonpathogenic. Others are capable of causing severe infections. Most severe infections are due to *Staphylococcus aureus*. As a rule, *Staphylococcus albus* is less pathogenic than *Staphylococcus aureus* and *Staphylococcus citreus* has little pathogenic activity. As a whole, lower animals are less susceptible to staphylococcus infections than man. One variety of anaerobic staphylococcus may occasionally cause puerperal fever. Since *Staphylococcus albus* and *Staphylococcus citreus* closely resemble *Staphylococcus aureus*, which is much more important, the remainder of this discussion will be directed primarily toward the latter organism.

Toxic Products of Staphylococci.—Among the products having some of the characteristics of toxins produced by different strains of staphylococci are those that (1) destroy red blood cells (hemolysins), (2) destroy leucocytes, (3) cause necrosis of tissue, (4) produce death, and (5) cause gastroenteric symptoms. Probably no single strain produces all of these poisons and many produce none of them.

Sources and Mode of Infection.—Staphylococci are normal inhabitants of the skin, mouth, and nose of man. They usually live in these areas without causing disease, but once past the barrier offered by the skin and mucous membrane they are capable of causing extensive disease. They may pass through the unbroken skin under certain conditions. The natural invasive characteristics of staphylococci and the resistance of the body are so well balanced that infection probably never occurs unless a highly virulent organism is encountered or the body resistance is lowered.

Diseases Caused by Staphylococci.—Among the important diseases that may be caused by staphylococci are pustules, furuncles (boils), abscesses, carbuncles, and infections of surgical wounds. They are one of the causes of empyema, cystitis, and pyelitis. They are the most common cause of acute and chronic osteomyelitis and some forms of impetigo contagiosa. Staphylococci are occasionally the cause of

meningitis. Some of these cases recover. *Staphylococcus septicemia* is characterized by the formation of metastatic abscesses in different parts of the body, severe symptoms, and a high mortality. *Staphylococcus septicemia* may occur as a primary condition, but in most cases it is due to an invasion of the blood stream by organisms from a localized site of infection. Boils about the nose and lip are especially liable to be followed by septicemia, and for this reason should not be subjected to such procedures as squeezing, etc. Stitch abscesses are usually due to *Staphylococcus albus* which is a normal inhabitant of the skin. *Staphylococcus* food poisoning has been discussed previously.

Bacteriological Diagnosis.—A bacteriological diagnosis of a staphylococcus infection is usually easily made by means of smears and cultures. In making blood cultures for staphylococci, special pains should be taken to exclude those inhabiting the skin.

Immunity.—Man possesses considerable natural immunity to staphylococci. Persons who have debilitating diseases, especially diabetes, are more susceptible to staphylococcus infections than are normal persons. *Staphylococcus* infections are not followed by any detectable immunity, but at least some degree of active immunity can be established by artificial means.

Specific Therapy.—Vaccines prepared by killing staphylococci with heat give good results in chronic infections. Autogenous vaccines, i.e., vaccines prepared from the lesions of the patient, give better results than stock vaccines. *Staphylococcus* toxoid seems to give good results in recurrent boils. *Staphylococcus* antitoxin is coming into use in treating severe staphylococcus infections, especially when accompanied by toxic manifestations.

IV. *Micrococcus Tetragenus*

This is a large gram-positive organism that resembles the staphylococcus but occurs in groups of four. It is sometimes found in the saliva of healthy persons and is often associated with cavity formation in pulmonary tuberculosis.

Questions for Review

1. What is the Neufeld test? Why has its importance decreased?
2. Name ten diseases of man caused by streptococci and give the type of organism most often responsible for each disease.
3. How are streptococci conveyed from person to person?
4. How is a streptococcus infection prevented?
5. Discuss the source and mode of infection in scarlet fever.
6. What is the basis of the Dick test?
7. What is septic sore throat? What is its cause?
8. What is *Micrococcus tetragenus*? What is it associated with?

True-False Test

Place the word "true" or "false" before each statement.

- 1. The pneumococcus is very susceptible to ordinary germicides.
- 2. A bacteriemia is never present in pneumonia.
- 3. Pneumococci enter and leave the body by the same route.
- 4. Practically every person becomes a carrier of pneumococci at some time during the year.
- 5. Recovery from a pneumococcus infection confers a permanent immunity.
- 6. A person with pneumonia need not be isolated.
- 7. Streptococci are probably responsible for more illness than any other group of organisms.
- 8. Streptococcus meningitis is fatal in practically 100 per cent of cases.
- 9. Streptococcus infections are never followed by an immunity.
- 10. It is believed that scarlet fever may be caused by any of the hemolytic streptococci belonging to Lancefield's group A.
- 11. Erysipelas is an acute inflammation of the deeper layers of the skin due to hemolytic streptococci.

Completion Test

1. Pneumonia occurs in two forms: ----- and -----.
2. There are ----- types of pneumococci.
3. Pneumococci are gram-----.
4. The most fatal type of pneumococcus is type -----.
5. Cases of pneumonia that are not due to the pneumococcus may be due to B. ----- or -----.
6. What are the three types of streptococci based on their action on blood agar?
 - a. -----
 - b. -----
 - c. -----

Which type is the most virulent? -----

7. Poisons produced by streptococci are _____,
_____, _____, and
_____.
8. The _____ test is valuable in the differentiation
of scarlet fever from measles, erythema, and urticara.
9. The general characteristics of staphylococci are _____,
_____, and _____.
10. Based on the color of pigment produced when grown on artificial
media, staphylococci may be classified as _____,
_____, and _____.

References

- Rosenau, Milton J.: Preventive Medicine and Hygiene, New York, 1935, D. Appleton-Century Co.
- Henry, J. Norman: A Study of Active Immunization Against Scarlet Fever in Charitable Institutions and Public Schools of Philadelphia, *J. A. M. A.* 105: 488 (Aug. 17), 1935.
- Smillie, Wilson G.: Preventive Medicine and Public Health, New York, 1946, The Macmillan Company.
- Schaub, Isabelle G., and Foley, M. Kathleen: Methods for Diagnostic Bacteriology, St. Louis, 1947, The C. V. Mosby Company.
- Topley and Wilson: Principles of Bacteriology and Immunology, Baltimore, 1946, Williams & Wilkins Co.

CHAPTER XXVI

THE GRAM-NEGATIVE COCCI

The most important gram-negative cocci are the gonococcus and meningococcus. *Micrococcus catarrhalis* is of importance not on account of its pathogenic effects but because it is of such common occurrence in the locations in which the other two organisms are found and resembles them so closely that its differentiation from them becomes a laboratory procedure of importance.

I. The Gonococcus

The gonococcus is the cause of gonorrhea, one of the three great venereal diseases (gonorrhea, syphilis and chancroid*). It is sometimes called the diplococcus of Neisser after its discoverer, and infections due to it are often spoken of as Neisserian infections. This organism is known also as *Micrococcus gonorrhoeae*, *Diplococcus gonorrhoeae*, and, more properly, *Neisseria gonorrhoeae*.

General Characteristics.—The gonococcus is a gram-negative nonmotile, nonspore-forming diplococcus. In smears the opposing sides of the two cocci are flattened which gives them the appearance of two coffee beans lying with their flat sides together. Gonorrhea is accompanied by a discharge which is at first serous then purulent. During the early stages the gonococci are found free in the serum or attached to epithelial cells, but when the exudate becomes purulent phagocytosis takes place and the gonococci are found within the cytoplasm of the pus cells (polymorphonuclear leucocytes). A single cell may contain from 20 to 100 gonococci. These gonococci are not dead, which is proved by the fact that they are capable of causing infection. In later stages of the disease they may be found outside the cells, and when the disease becomes chronic they often cannot be found at all.

*In addition there are two less important venereal diseases: granuloma inguinale and venereal lymphogranuloma (lymphogranuloma inguinale). The former is an ulcerative condition, in the lesions of which cell inclusions known as Donovan bodies are found. The latter is an inguinal adenitis due to a filtrable virus.

The gonococcus will not grow on ordinary culture media and is somewhat difficult to cultivate even on media prepared especially for its propagation. Gonococci grow best at or slightly below body temperature and in the presence of oxygen. Although gonococci grow in the presence of oxygen, they grow best in an atmosphere of which the oxygen content is slightly less than that of ordinary air.



Fig. 87.—Urethral pus showing gonococci. The small structures are gonococci. They are seen lying chiefly in the cytoplasm of the polymorphonuclear leucocytes. The large dark structures within the cells are nuclei. (From Ford: *Textbook of Bacteriology*. W. B. Saunders Co.)

Although gonococci are difficult to destroy within the body, they possess little resistance outside the body. They are killed in a very short time by sunlight and drying. When incorporated in pus under conditions most suited for the maintenance of their vitality, they do not survive more than a day. They are very susceptible to disinfectants, especially silver salts, and are killed by a temperature of 60° C. within ten minutes. Many strains are susceptible to

the action of the sulfonamide compounds and the great majority of the strains are susceptible to the action of penicillin.

All gonococci are not exactly alike from the immunological standpoint but represent a great number of closely related subgroups.

Pathogenicity.—The gonococcus is an organism specifically parasitic for man. Spontaneous infection does not occur in lower animals and nothing comparable to any of the clinical forms of gonorrhea has been produced in them by artificial means. In man gonorrhea usually begins as a urethritis from which the infection may spread to various parts of the body. A less common but important site of primary infection is the conjunctiva. About 60 per cent of cases of conjunctivitis in the newborn (ophthalmia neonatorum) are due to the gonococcus. Infants and children are much more susceptible to gonorrheal infections of the conjunctiva than are adults. Gonorrheal vulvovaginitis of little girls may occur in epidemic form.

Gonococcus infections have a tendency to become chronic and in some cases a person may remain capable of transmitting the infection to others months or years after symptoms have disappeared.

Sources and Mode of Infection.—Gonococci are never found outside the human body unless they are on objects recently contaminated with gonorrheal discharges, and here they live only for a short time. Therefore, gonorrheal infections are practically always spread by direct contact, and in the great majority of cases the mode of contact is sexual intercourse. It is not to be denied that gonorrhea is sometimes transmitted indirectly by contaminated towels, etc., but it certainly is not a common way. Gonorrheal ophthalmia of adults is usually due to the transmission of infection from the patient's genitourinary tract to his eyes by his hands. In infants it is contracted while passing through the birth canal. Epidemic vulvovaginitis in children is spread by the use of common bed linen, bathtubs, etc. It usually occurs where children live in closely crowded quar-

ters. Vulvovaginitis may occur sporadically, in which case it is probably most often contracted from a toilet, recently contaminated linen, or by sleeping in a bed occupied by a person with gonorrhea.

Spread of Gonorrhea in the Body.—In typical cases of gonorrhea in the female the site of primary infection is the urethra and cervix; in the male it is the urethra. Vaginal infection in adults is not common because the epithelium lining the vagina of adults is of the stratified squamous type which is resistant to infection with gonococci. Before the age of puberty the vagina does not have this type of lining and is susceptible to infection. The changes in vaginal epithelium incident to puberty may eradicate a childhood infection. From the urethra of the male the infection may spread by direct extension to the epididymis, seminal vesicles, prostate, bladder, and periurethral glands. In the female it may spread by direct extension to Bartholin's glands, the bladder, and fallopian tubes. The endometrium seems to be resistant to the action of gonococci. From the fallopian tubes the infection often spreads to the ovaries, and in rare cases to the peritoneum. Infection of the rectum may occur in the female as a result of the forcing of vaginal secretions upon the everted rectal mucosa during defecation. Fortunately, the vulvovaginitis of children has little tendency to spread to other parts of the body. Scarring caused by gonococcus infections of the urethra often leads to stricture.

Gonococci may enter the blood stream and cause a septicemia with or without endocarditis. More often they localize in the joints and cause an arthritis. Gonorrheal iritis is not uncommon. More rarely sciatica, neuralgia of the nerves terminating in the infected parts, and meningitis are due to the action of gonococci.

Laboratory Diagnosis.—The bacteriologist has at his command three procedures applicable to the diagnosis of gonorrhea: namely, (1) smears, (2) cultures, and (3) the complement fixation test. There are rare exceptions to the rule, but for all practical purposes the finding of gram-negative intracellular diplococci in the exudate from a genital infec-

tion means that the organisms are gonococci and this is especially true if the exudate is from the male urethra. Remember that gram-negative diplococci other than gonococci frequently occur outside the cells, while gram-positive organisms having the morphology of gonococci may occur within the cells. All that can be said about gram-negative diplococci occurring outside the cells is that they *may be* gonococci. Gram-negative diplococci other than gonococci may occasionally be found within the pus cells of a genital exudate, but this is so infrequent that it has little tendency to weaken the correctness of considering all such organisms gonococci. In the exudate of chronic gonorrhea the organisms are more often not found than found. Within recent years the methods of cultivating gonococci have undergone great improvement and cultural methods have assumed a place of practical value in the diagnosis of gonorrhea. Cultural methods are of special value in the diagnosis of chronic gonorrhea and in the determination of a cure.

The complement fixation test for gonorrhea, which differs from the complement fixation test for syphilis (Wassermann test) only in the antigen used, is often positive in gonorrheal septicemia or chronic infections but is uniformly negative in acute localized infections. The highest percentage of positive results is obtained in gonorrheal septicemia, rheumatism, and iritis. The percentage of positive results in gonorrhea is not as high as the percentage of positive Wassermann tests in syphilis.

It is never within the province of the laboratory alone to say that a person is cured of gonorrhea, and in many cases the efforts of both laboratory and clinician are incapable of determining whether or not the disease is completely eradicated.

Economic and Social Importance of Gonorrhea.—It has been reliably estimated that about 10 per cent of the general population have some venereal disease. Of these about two-thirds have gonorrhea. The most destructive piece of misinformation that has been handed down from generation to generation is that gonorrhea "is no worse than a cold."

It both underestimates the danger of gonorrhea and creates the impression that colds are of little importance. As a matter of fact, gonorrhea is equal to, if not greater than, syphilis as a cause of chronic ill health and is just as difficult to cure. Like syphilis, it is a disease of youth and often condemns a person to invalidism during the years he should be most useful. Gonorrhea is one of the causes of sterility in both male and female. It is responsible for from 70 to 80 per cent of gynecological diseases, especially salpingitis, and in the majority of cases the infection was contracted from a husband who thought himself cured. Gonorrheal ophthalmia may be followed by blindness. Not only does gonorrhea bring about the conditions enumerated above, but it lowers general body health, lessens economic efficiency, and promotes an improper mental attitude.

Immunity.—An attack of gonorrhea confers little, if any, immunity to subsequent attacks. Vaccines and serums have been used to establish immunity in gonorrhea but their results have not been particularly convincing.

Prevention.—The general public should be informed of the dangers of gonorrhea and the difficulty of its cure. The danger of quack doctors and folk remedies should be stressed. The patient should be taught that he should not allow his discharges to contaminate toilets or articles used by others. He should be warned of the danger of transferring the infectious material by means of his hands to his eyes. Immediately after birth, the eyelids of the child should be cleansed with a saturated solution of boric acid. A different piece of cotton should be used for each eye and the lids should be stroked from the nose outward. Next the lids are opened and one or two drops of 1 per cent silver nitrate are instilled into each eye, care being taken that the conjunctival sac is completely covered with the solution. This is known as Crede's method. It is so important that failure to apply it in each and every case is inexcusable. Vulvovaginitis in children may be prevented by proper care of bed linen, bathtubs, night clothes, wash water, etc., and by examination of all children for gonorrhea before admitting them to children's institutions or hospital wards for children.

II. The Meningococcus

The meningococcus (*Diplococcus meningitides* of Weichselbaum) is the cause of meningococcus septicemia with or without localization in the meninges to produce epidemic cerebrospinal meningitis. Epidemic cerebrospinal meningitis is known also as cerebrospinal fever, spotted fever, and meningococcus cerebrospinal meningitis. The nonepidemic forms of meningitis will be discussed on page 624.

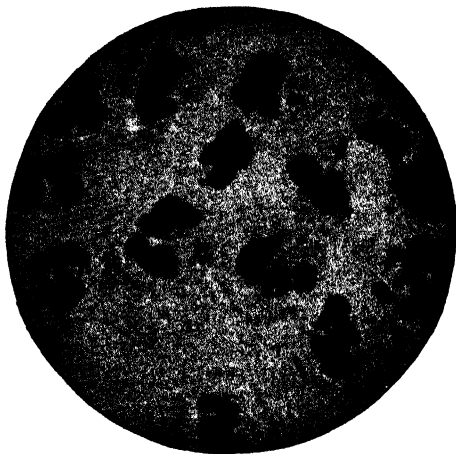


Fig. 88.—Meningococci in smear from cerebrospinal fluid. Note pale cocci lying in cytoplasm of polymorphonuclear leucocytes. (From Gradwohl: *Clinical Laboratory Methods and Diagnosis*. The C. V. Mosby Co.)

General Characteristics of the Meningococcus.—Meningococci are gram-negative diplococci that have a marked resemblance to gonococci but show more irregularity in size and shape. They are nonmotile and do not form spores. In the spinal fluid they appear both within and without the polymorphonuclear leucocytes. They are found in the extracellular position most often in severe cases that are not doing well. It is necessary to know the source of the specimen to determine whether gram-negative intracellular diplococci found in a smear are meningococci or gonococci.

Meningococci grow best at body temperature under aerobic conditions. They do not grow at room temperature. Growth occurs only on special media containing such enriching sub-

stances as whole blood, blood serum, or ascitic fluid. Agar containing laked rabbit blood and dextrose support the growth of meningococci specially well, and the same is true of hormone agar containing enriching substances. Different strains of meningococci show considerable variation in the ease with which they grow on artificial culture media.

Meningococci are such frail organisms that they survive only a short time outside the body. Sunlight and drying kill them within twenty-four hours. They are easily killed outside the body by ordinary disinfectants, but in the nasopharynx they are very resistant to their action. Like gonococci they are especially susceptible to the action of methylene blue. They are very susceptible to heat. In cerebrospinal fluid meningococci quickly undergo solution. Therefore, specimens of fluid suspected of containing meningococci should be examined as quickly as possible. Salt has a toxic effect on meningococci and should not be put in media on which they are to be cultivated.

Meningococci and Gonococci Compared.—Meningococci and gonococci are much alike in that: (1) both are strict parasites and cause disease only in man, (2) they show little difference in resistance to injurious agents, (3) their distribution in the inflammatory exudate is the same, and (4) they grow on artificial media with difficulty. It may be said that they are morphologically, physiologically, and immunologically very much alike. The immunological resemblance is due to the presence of common antigenic substances in both organisms.

Types of Meningococci.—Different strains of meningococci fall rather definitely into four immunological types (Types I, II, III, and IV). Of these, Type I is most common. It appears that Types I and III and Types II and IV are closely related.

Toxin Production.—Most observers believe that meningococci do not produce exotoxins but do produce endotoxins which are liberated when the cocci disintegrate and that these toxins are at least partly responsible for the symptoms of meningitis. Others believe that when grown in suitable

broth cultures, meningococci liberate true exotoxins. The majority, however, believe that these toxins are in truth endotoxins liberated by the autolysis of the meningococci which occurs with extreme rapidity when the organism is grown in a liquid medium. Regardless of whether meningococci produce true exotoxins or only endotoxins, immunization of horses with the filtrate of a broth culture of meningococci (if the broth is of the proper kind) yields a serum containing an abundance of antitoxic substances.

Pathogenicity.—The meningococcus is not very pathogenic for the lower animals and typical cerebrospinal fever occurs only in man. The modern idea of cerebrospinal fever is that it is primarily a septicemia with subsequent localization of the organisms in the meninges. At least, the organisms are found in the blood during the early days of the disease. The essential meningeal change characteristic of epidemic meningitis is a purulent inflammation of the meninges that has a tendency to localize along the base of the brain and in the upper end of the spinal cord. Cases of meningococcus septicemia without subsequent meningeal localization very often prove fatal.

Source and Mode of Infection.—Since meningococci are such frail organisms and are seldom found outside the body, the source of infection must be a patient or a carrier. The organisms are found in the nasopharynx of both patients and carriers and leave the body in the nasal and buccal secretions. The mode of transfer is usually by rather close contact and the organisms enter the body by the nose and mouth. When meningococci reach a new host they localize in the nasopharynx and multiply. From the nasopharynx they enter the blood stream, producing a septicemia. The septicemia may or may not be followed by localization in the meninges (cerebrospinal meningitis), joints, skin, or other body tissues. It was formerly thought that meningococci passed directly from the nasopharynx to the meninges. This mode of transfer is now seriously questioned. Infection due to articles recently contaminated by infected nasal and buccal secretions is not impossible but seldom occurs.

Meningococcus infection is not highly communicable. Of those exposed to a case, many become carriers but few develop the disease. Meningococcus infection is endemic in all highly populated centers and may become epidemic under conditions of overcrowding as occurs most often in army camps, etc. Next to pneumonia it is the most serious disease to be dealt with in the mobilization of troops.

It has been estimated that under ordinary conditions from 2 to 5 per cent of the general population are carriers of meningococci. When epidemics occur the number of carriers increases. About two-thirds of those who contract meningitis harbor the organisms for a variable time after convalescence. Healthy persons who have never had meningitis but nevertheless harbor meningococci in their nasopharynx play a more important part in the spread of meningitis than those who harbor the organisms after recovery from the disease. Carriers may be made meningococcus-free by the administration of sulfadiazine.

Immunity.—If most people did not have a comparatively high immunity to meningococci, the great number of carriers in the general population would maintain an epidemic at all times. That epidemics are not more common than they are is due to the fact that while nasopharyngeal infection is common, general infection occurs only in those whose resistance to meningococci is low. Overcrowding increases infection by increasing the number of carriers and promoting those conditions that tend to bring about a general lowering of resistance. Negroes are more susceptible to meningitis than whites. One attack of the disease does not protect against subsequent attacks. The injection of vaccines leads to the production of bacteriolysins and agglutinins.

Laboratory Diagnosis.—In order to give the patient the advantage of early treatment, which means so much in meningococcus infections, meningococcus septicemia should be diagnosed on clinical grounds. The diagnosis may be confirmed by blood cultures. A valuable diagnostic adjunct is the demonstration of meningococci in the skin lesions by smears or cultures. In epidemic meningitis the cerebro-

spinal fluid is usually turbid then purulent. The typical arrangement of gram-negative diplococci within the cells is sufficient for practical purposes to make a diagnosis of epidemic meningitis. In severe cases in which the patient is not doing well the organisms may be found wholly outside the cells. On account of the tendency of the organisms to undergo solution the specimen should be examined as quickly as possible after it is withdrawn. For the same reason a cerebrospinal fluid that shows many pus cells but no organism suggests the presence of cerebrospinal meningitis. Carriers are detected by special cultural methods which the student will find discussed in books on bacteriology more advanced than this one.

Specific Therapy.—Before the advent of the sulfonamide compounds and penicillin, the mainstay in the treatment of epidemic meningitis was antimeningococcus serum, which was of two types, bactericidal and antitoxic. The bactericidal serum which is the common type that has been in use for a long time is prepared by giving horses a series of injections of several different strains of organisms representing the important groups of meningococci. The antitoxic serum (antitoxin) is prepared by passing the proper kind of liquid culture of meningococci through a bacteria-retaining filter and immunizing horses with the bacteria-free filtrate. Although the use of antimeningococcus serum reduced the mortality in epidemic meningitis, its results did not equal those which are now obtained with the sulfonamide compounds and penicillin. Vaccination with killed meningococci gives rise to some degree of antibody formation.

Prevention.—General preventive measures are the avoidance of overcrowding and the proper supervision of carriers. The wholesale isolation of carriers has not proved successful in the prevention of infection, and the trend at the present time is to isolate only those in immediate contact with a case. The general use of nose sprays, etc., is probably of little value. Vaccination with dead meningococci probably has enough preventive value to be resorted to in times of epidemics.

The patient with a meningococcus infection should be isolated and should remain in isolation until cultures fail to show meningococci in his nasopharynx. All discharges from the mouth and nose and articles soiled therewith should be disinfected. The urine occasionally contains the organisms and therefore should be disinfected. The physician and nurse should use every precaution to prevent themselves from becoming infected or acting as carriers. This may be partially accomplished by occasionally spraying the mouth and nose with 10 per cent argyrol. The nurse should exercise care lest her hands convey the infection. Dishes used by the patient should be properly sterilized. People who have been in close contact with a case of meningitis should not be allowed to mingle with others until bacteriological examination has proved them to be free of meningococci.

Regardless of what measures we may take, epidemic meningitis remains a disease, the control of which is yet to be accomplished. For reasons which we do not understand, it suddenly becomes virulent in a community, attains epidemic form, persists for a time and, for other reasons which we do not understand, disappears.

III. *Micrococcus Catarrhalis*

These organisms are normal inhabitants of the mucous membranes, especially of the respiratory tract. They may cause a mild catarrhal inflammation under certain conditions but are of greatest importance to the bacteriologist on account of their likelihood of being confused with meningococci or gonococci. Like these organisms they are gram-negative, biscuit-shaped diplococci and on rare occasions may assume the intracellular position. Differentiation depends on agglutination tests and the ability of *M. catarrhalis* to grow on ordinary culture media at room temperature.

Questions for Review

1. What are the sources and mode of infection in gonorrhea? How is gonorrheal ophthalmia contracted in adults? In infants?
2. What are the sources and mode of infection in cerebrospinal meningitis?

3. Discuss the prevention of meningitis.
4. How long should a patient with epidemic meningitis remain in isolation? Give the nursing precautions.

True-False Test

Place the word "true" or "false" before each statement.

- 1. Infants and children are much more susceptible to gonorrheal infections of the conjunctiva than are adults.
- 2. Gonococci may enter the blood stream and cause a septicemia.
- 3. It is never difficult to determine when a case of gonorrhea is cured.
- 4. Cultural methods are of special value in the diagnosis of chronic gonorrhea.
- 5. It has been proved that gonorrhea never causes sterility.
- 6. Meningococci resemble gonococci.
- 7. Meningococci are easily killed outside the body by ordinary disinfectants.
- 8. Meningococcus carriers are very difficult to rid of their organisms.

Completion Test

1. The gonococcus is gram- -----.
2. The gonococcus was discovered by -----.
3. The gonococcus is very ----- to destroy outside the body.

References

- Pelouz, P. S.: *Gonorrhea in the Male and Female*, Philadelphia, 1941, W. B. Saunders Co.
- Daniels, W. B., Solomon, Sydney, and Jaquette, W. A.: *Meningococcal Infection in Soldiers*, J. A. M. A. 123: 1 (Sept. 4), 1943.
- Smillie, Wilson G.: *Preventive Medicine and Public Health*, New York, 1946, The Macmillan Co.
- Topley and Wilson: *Principles of Bacteriology and Immunology*, Baltimore, 1946, Williams & Wilkins Co.

CHAPTER XXVII

THE HEMOGLOBINOPHILIC BACILLI

All bacilli that do not grow in pure cultures except on media that contain hemoglobin or a similar substance are known as "hemoglobinophilic bacilli." This genus of organisms is known as genus *Hemophilus*.

I. The Influenza Bacillus (*Hemophilus Influenzae*)

In 1892 Pfeiffer described a bacillus, now known as *Pfeiffer's bacillus*, *B. influenzae*, or *Hemophilus influenzae*, which he found in the sputum of patients with influenza.

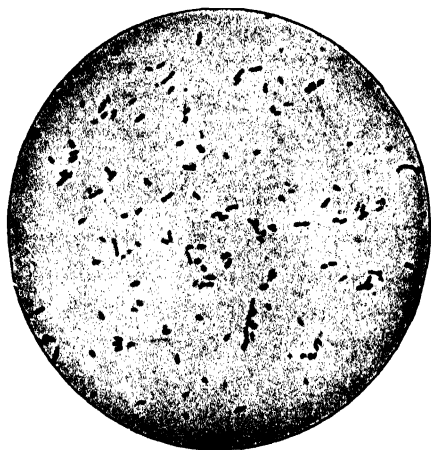


Fig. 89.—*Hemophilus influenzae*. (From Park and Williams: *Pathogenic Microorganisms*. Lea and Febiger.)

Until the 1918-1919 pandemic this bacillus was regarded as the sole cause of influenza. At that time its etiological importance began to be questioned and it is now known that the primary cause of influenza is a filtrable virus or viruses. *H. influenzae* still maintains a position of importance, however, because in addition to being a common secondary invader in influenza and certain other respiratory diseases, it may be the primary cause of meningitis, otitis media, and sinusitis.

Characteristics of *H. Influenzae*.—*H. influenzae* is the smallest known pathogenic bacillus. It grows best in the

presence of oxygen but may grow in its absence. It is non-motile and does not form spores. It does not occur outside the body and is very susceptible to destructive influences. It is slightly susceptible to the action of the sulfonamide compounds and penicillin. It is more susceptible to streptomycin. Influenza bacilli grow only on special media. Growth is often more luxuriant when certain other organisms as *Staphylococcus aureus* are present.

H. influenzae is moderately pathogenic for the lower animals, especially the rabbit. In man it causes bronchopneumonia and may sometimes invade the blood stream. *H. influenzae* meningitis occurs most often in children. It is characterized by its high mortality. Recently, Alexander has prepared an anti-*H. influenzae* serum from rabbits, which when combined with the sulfonamide compounds results in a high percentage of recovery in cases of meningitis caused by *H. influenzae*. *H. influenzae* is found in the throats of about 30 per cent of normal persons.

II. The Pertussis Bacillus (*Hemophilus Pertussis*)

Whooping cough (pertussis) is a communicable disease that chiefly affects children and is characterized by a catarrhal inflammation of the respiratory tract with a paroxysmal cough that ends in a whoop. It is a widespread and dangerous disease that is one of the major causes of death in young children. Its danger lies in the frequency with which it is complicated by bronchopneumonia, or malnutrition, or such chronic diseases as tuberculosis that follow in its wake. Twenty-five per cent of the children who have whooping cough before they are one year old die, usually from a complicating bronchopneumonia. The general mortality is 15 per cent. It is one of the most important causes of death from communicable diseases in children under five years of age, and it is during this period that 90 per cent of the deaths from whooping cough occur. Unfortunately these facts do not seem to be generally recognized.

There have been many agents accused of being the cause of whooping cough, prominent among which was and is a filtrable virus. The weight of evidence points almost con-

clusively toward a bacillus which was observed in the sputum of patients with whooping cough by Bordet and Gengou in 1906. They named this organism *B. pertussis*, but it is often spoken of as the Bordet-Gengou bacillus and is now more properly known as *Hemophilus pertussis*.

Characteristics of *H. Pertussis*.—*H. pertussis* is a small gram-negative bacillus that bears a close resemblance to *H. influenzae*. It shows polar staining, is nonmotile, and does not form spores. It grows best in the presence of oxygen but may grow under anaerobic conditions. It is not affected by the sulfonamide compounds and penicillin. It is susceptible to the action of streptomycin. When freshly isolated from the body, *H. pertussis* grows only on special media containing blood. A medium that is especially suitable for its cultivation is glycerin-potato-blood agar. It grows slowly on artificial media, two or three days often elapsing before the growth becomes visible.

Pathogenicity.—*H. pertussis* is distinctly pathogenic for lower animals, especially rabbits and guinea pigs. In the respiratory system of man the bacilli produce their effects by aggregating between the cells and on the walls of the trachea and bronchi. It seems that the action of *H. pertussis* is, at least in part, due to a toxinlike substance which it produces. This toxin appears to partake of the nature of both endotoxins and exotoxins. The organism does not invade the blood stream.

Mode of Infection.—Whooping cough is usually transmitted by direct contact and droplet infection but may be transmitted by recently contaminated objects. The disease is communicable during any stage and often during convalescence. The period in which the child is most likely to spread the infection begins before the "whoop" appears and lasts about three weeks. Whooping cough is one of the most highly communicable of all diseases. The bacilli enter the body by the mouth and nose and are thrown off in the buccal and nasal secretions. With the exception of those who have been closely associated with the disease or those convalescent from the disease, carriers do not exist. Convaless-

cent carriers, in the great majority of cases, become non-infectious soon after the subsidence of the disease.

Diagnosis.—The most effective method of bacteriological diagnosis of whooping cough is known as the “cough plate method” in which an open Petri dish containing glycerin-potato-blood agar medium is held in front of the mouth of the child during a paroxysm of coughing. The organisms are sprayed on the medium by droplets from the mouth and nose. After the “plates” are incubated for about three days, a visible growth appears. In some instances, possibly 5 per cent of cases, a disease clinically indistinguishable from whooping cough has been found to have an organism other than *H. pertussis* associated with it.

Immunity.—Man possesses no natural immunity to whooping cough. An attack is usually followed by a permanent immunity. Second attacks, except in the aged, are usually mild. The mother does not transmit immune bodies to her offspring. Therefore, the newborn child does not enjoy an immunity to whooping cough as he does to a number of other diseases.

Specific Therapy.—Properly selected and properly administered, pertussis vaccines have a distinct preventive value. Their curative value is open to debate. Theoretically they should have little or no curative value. Practically, according to many observers, the opposite is the case. Convalescent serum or the serum of an adult recently vaccinated against the disease seems to be of distinct value in preventing infection of those exposed and in reducing the severity of symptoms in those already ill. An antipertussis serum made from rabbits has been used with success as both a preventive and a therapeutic agent in very young children.

Prevention.—Whooping cough itself can scarcely be prevented by our present public health methods, but its death rate can be reduced to a remarkable degree. Mothers should be taught how deadly a disease whooping cough is among young children and that every possible means should be used to prevent them from becoming exposed, because the older the child the less the danger of a secondary bronchopneumonia. The infected child should be isolated and should

remain in isolation for several weeks after the whoop has disappeared. The child need not be kept in bed but should be allowed to play in the sunshine and fresh air. In other words, a child with whooping cough should have free access to his own back yard, provided weather conditions are suitable, but other children should stay away. The child should be immunized with pertussis vaccine as early as possible, i.e., between the sixth and ninth month. Many pediatricians believe that the immunization of mothers during the last months of pregnancy results in the placental transfer of sufficient antibodies to protect the newborn infant.

III. The Bacillus of Ducrey

Ducrey's bacillus, or *Hemophilus ducreyi*, is the causative organism of chancroid. Chancroid is a local, highly contagious, venereal ulcer that has no relation to chancre, the initial lesion of syphilis. Chancroid usually begins as a pustule that ruptures, leaving an ulcer with undermined edges and a gray base. The ulcers spread rapidly and are usually multiple. They do not have indurated edges, as is the case with chancres, hence chancroids are often spoken of as "soft chancres." The infection often spreads to the inguinal lymph nodes, producing abscesses known as "buboes." The organism can be cultured only by special methods. It is rather susceptible to antiseptics. The infection responds to sulfadiazine. It does not respond so well to penicillin. The chancroidal ulcer must be differentiated from the chancre of syphilis, and the buboes must be differentiated from those of granuloma inguinale and lymphopathia venereum.

Chancroid is usually transmitted by sexual intercourse but may be transmitted by surgical instruments, dressings, etc. Treatment should be carried out with great care on account of the serious complications that may occur. About one-half of venereal ulcers are mixed chancres and chancroids.

Recently an intradermal test for the differentiation of chancroids from other venereal ulcers has been devised. It consists of the intradermal injection of a saline suspension of *H. ducreyi*. A positive result is indicated by an area of

redness and induration at the site of injection. The reaction usually reaches its maximal intensity at the end of 48 hours. This test has been used extensively in European countries.

IV. Other Hemoglobinophilic Bacteria

Koch-Weeks Bacillus.—This bacillus is the cause of “pink eye,” a form of conjunctivitis that has a marked tendency to occur in epidemics. Other names for the bacillus are *B. conjunctivitis* and *Hemophilus conjunctivitis*. The disease is transferred by hands, towels, handkerchiefs, etc. When the disease is introduced into a group of people, a high percentage becomes infected.

Morax-Axenfeld Bacillus.—This organism causes an acute or chronic inflammation of the conjunctiva, eyelids, and cornea. Infections with this organism do not respond to treatment with silver salts.

Questions for Review

1. How does the causative agent of pertussis enter and leave the body?
2. During what stage of the disease is a child with whooping cough most likely to transmit the infection to others?
3. Discuss the prevention of pertussis.

True-False Test

Place the word “true” or “false” before each statement.

- 1. *H. influenzae* is the smallest known pathogenic bacillus.
- 2. Whooping cough is a highly communicable disease.
- 3. Pertussis confers an immunity of short duration.
- 4. Carriers of pertussis bacilli are frequently found.

Completion Test

1. *H. influenzae* may be the primary cause of _____, _____, and _____.
2. About _____ per cent of normal persons have *H. influenzae* in their throats.
3. All bacilli that do not grow in pure cultures except on media that contain hemoglobin or a similar substance are known as “_____” bacilli.
4. Pertussis is frequently complicated by _____.
5. At what age is whooping cough most dangerous? _____.
6. Whooping cough is usually transmitted by _____ contact.

7. The most effective method of bacteriological diagnosis of whooping cough is known as the "-----" method.
8. Ducrey's bacillus is the causative organism of -----.
9. Is there an intradermal test for the differentiation of chancroid from other venereal ulcers? -----

References

- Francis, Thomas: Recent Advances in the Study of Influenza, J. A. M. A. 105: 251 (July), 1935.
- Sauer, Louis: The Known and Unknown of Bacillus Pertussis Vaccine, Am. J. Public Health 25: 1226 (Nov.), 1935.
- Kendrick, Pearl, and Eldering, Grace: Progress Report on Pertussis Immunization, Am. J. Public Health 26: 8 (Jan), 1936.
- Smillie, Wilson G.: Preventive Medicine and Public Health, New York, 1946, The Macmillan Company.

CHAPTER XXVIII

MISCELLANEOUS BACTERIA AND BACTERIAL INFECTIONS

I. Anthrax

Anthrax is an acute infectious disease caused by *B. anthracis*. It is primarily a disease of lower animals, especially cattle and sheep, but it is easily communicated to man. In man it occurs in two forms: *external anthrax* (malignant pustule or carbuncle and anthrax edema) and *internal anthrax* (pulmonary anthrax or wool sorters' disease and intestinal anthrax). Malignant pustule is the most common form; intestinal anthrax is the least common. Because of the fever and enlargement of the spleen that accompanies the disease, anthrax is often called splenic fever.

The Anthrax Bacillus.—*B. anthracis* is a large gram-positive organism of characteristic appearance. It is the only spore-forming aerobic pathogenic bacterium. It grows in the presence of oxygen and also when it is absent. Spores are not formed when oxygen is absent, and therefore are not formed in the animal body. Growth is luxuriant on all ordinary culture media. The organism is susceptible to the action of penicillin but is resistant to the action of the sulfonamide compounds. Spores retain their vitality for years and are extremely resistant to heat.

B. anthracis is of historical interest because it was the first pathogenic organism to be seen under the microscope, the first one proved to be the cause of a specific disease, and the first one to be grown in a pure culture.

Mode of Infection.—Animals usually become infected via the intestinal route while grazing in infected pastures. In man, anthrax is primarily an occupational disease confined to those who handle animals or their products, such as hair and hides. Imported animal products are of special danger. The most common route of infection is through wounds or abrasions of the skin. Numerous cases of anthrax

due to infection of the face by the bristles of cheap shaving brushes have been reported. Pulmonary anthrax occurs most often in those who handle dry hides, wool, or hair; it is caused by inhalation of dust containing the spores. Intestinal anthrax is acquired by drinking infected milk or eating insufficiently cooked infected food. The bacilli leave the body in the exudate of the local lesion (malignant pustule) and in the sputum, feces, and urine.



Fig. 90.—Anthrax bacilli. (From Zinsser and Bayne-Jones: *A Textbook of Bacteriology*, D. Appleton-Century Co.)

Specific Therapy.—Cattle and sheep may be actively immunized by vaccination. The vaccine contains living but attenuated bacteria. Dead bacteria are without effect. This method is not applicable to man. A therapeutic serum is prepared by immunizing horses against anthrax bacilli. It gives good results.

Prevention.—Patients with anthrax should be isolated. The dressings of external lesions should be burned. The

feces, urine, sputum, and other excreta should be disinfected at once in order to prevent the formation of spores. The disinfectant should be a strong one and should be applied for a long time. Five per cent carbolic acid is probably the best disinfectant. The local lesions of anthrax should not be disturbed by squeezing, etc., because this may cause the bacilli to invade the blood stream.

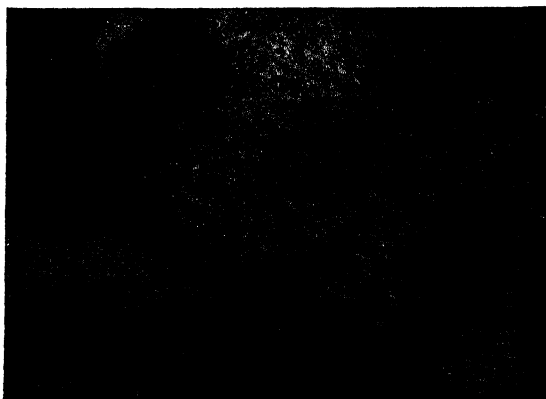


Fig. 91.—Anthrax lesion of neck. Probably contracted from infected shaving brush. (From Sutton and Sutton: *An Introduction to Dermatology*. The C. V. Mosby Co.)

Infected animals should be separated from the herd. The bodies of animals dead of anthrax should be burned if possible. Their blood should not be allowed to escape and their bodies should not be opened except for autopsy by an experienced veterinarian, because the bacilli will form spores when exposed to the air. If the body is buried, it should be packed with lime and should be buried at least three feet in the ground. When infection occurs in a herd, a sharp watch should be kept for new cases. Prophylactic vaccination of animals against anthrax should be carried out with vigor. Hides, hair, and shaving brushes should be sterilized to prevent their spreading infection.

II. Asiatic Cholera

Asiatic cholera is a specific infectious disease that affects the lower portion of the intestine and is characterized by

violent purging and vomiting, with muscular cramps, suppression of urine, and rapid collapse. Four great pandemics spread over the world during the eighteenth century.

Cause.—Cholera is caused by the cholera vibrio or the comma bacillus. This organism produces a powerful endotoxin. The disease is contracted by the ingestion of water or food that has been contaminated by the excretions of those harboring the bacilli. The bacilli leave the body in the feces, urine, and secretions of the mouth. As a rule, the feces become free of bacilli during the last days of the disease, but some patients become convalescent carriers. Permanent carriers are rare.

Immunity.—The immunity following an attack of cholera is of short duration. An active immunity may be established in about 90 per cent of cases by prophylactic vaccination. Members of the military personnel are given cholera vaccine upon being sent to duty in cholera-endemic areas.

The reader is referred to larger books for the geographical distribution and prevention of this disease.

III. Plague

Plague is an infectious disease due to *Pasteurella pestis* that primarily attacks rodents and is transferred from them to man. It occurs in two principal forms: the *bubonic* and *pneumonic*. The former is more common.

Many epidemics of plague have swept over great areas with a terrifying mortality (50 per cent or more). The disease exists in some part of the world at all times, and in these days of extensive travel and commerce must ever be guarded against. In our own country plague has been encountered in California, Texas, and Louisiana. The disease is endemic among the rodents of the western United States, and this focus of infection is an ever present and increasing source of danger because the infection is gradually spreading eastward. Plague among rodents is known as *sylvatic* plague (*sylvan*, wood). The hemorrhages that occur in bubonic plague and cause black splotches when affecting the skin, gave the name "black death" to plague during the Middle Ages.

Past. Pestis.—The plague bacillus belongs to the hemorrhagic septicemia group of organisms, infections with which cause areas of hemorrhage throughout the body. Other members of this group are the organisms of chicken cholera and swine plague. *Past. pestis* is a small aerobic, gram-negative organism that does not form spores. It grows on all ordinary media. Growth on agar containing from 3 to 5 per cent of salt is so characteristic as to be of importance in the recognition of the bacillus.

Plague bacilli may live outside the body in the carcasses of dead rats and in sputum for some time. They retain their vitality for months in the presence of moisture and in the absence of light. Five per cent carbolic acid or 1:1,000 bi-chloride of mercury solution destroys them in ten minutes. They are susceptible to the action of certain of the sulfonamide compounds.

Plague bacilli are highly pathogenic for many animals, including man, monkey, rats, mice, guinea pigs, and rabbits. They owe their action to endotoxins.

Clinical Types of Plague.—Plague occurs in two principal clinical types: the bubonic and pneumonic. In bubonic plague the organisms enter through the skin and are carried by the lymphatics to the lymph nodes draining the site of infection. Here the bacilli multiply and form abscesses of the nodes (buboes). Secondary buboes are formed in the nodes receiving drainage from the primary buboes, and the bacilli finally gain entrance to the blood stream, causing a septicemia. In pneumonic plague the symptoms are those of a bronchopneumonia, and the bacilli are found in abundance in the sputum. Only a very small percentage of cases in the average epidemic take the pneumonic form, but epidemics of strictly pneumonic plague may occur. Septicemic plague is a highly virulent form of plague in which the patient dies before buboes have time to develop.

Mode of Infection.—Although a number of rodents may be infected by *Past. pestis*, the one of greatest importance as a source of primary infection is the rat, and, as a rule, epidemics of human plague closely follow epidemics of rat plague. Plague is transmitted from rat to rat by the bite of

the rat flea. Man contracts the bubonic form of plague by the bite of a flea that has previously fed on an infected rat or, very much less often, an infected person. Just how the flea transmits the infection has not been definitely decided. Some workers believe that the bacilli are introduced into the body by material regurgitated while the flea is biting. Others hold that the bacteria-laden feces of the flea are deposited on the skin, and the organisms are implanted beneath the skin through minute abrasions caused by scratching, etc. Plague bacilli are found in the intestines of the flea where they are not only able to live for a long time but also to undergo rapid multiplication. Pneumonic plague may be due to an involvement of the lungs during the course of a bubonic plague (primary pneumonic plague) or to the inhalation of particles of sputum thrown off by a person with pneumonic plague (secondary pneumonic plague). Epidemic pneumonic plague is of the secondary type. Infection may occasionally be acquired by handling infected rodents. The disease is transmitted from locality to locality by infected rats. Rodents other than rats that may contract plague naturally are ground squirrels, marmots, and guinea pigs. There is some evidence that bedbugs and the human flea may transmit plague from person to person. The reason epidemics of human plague follow epidemics of rat plague is that, when an epidemic of rat plague occurs, the rat flea's food of first choice—the rat—is destroyed, and the flea then seeks his food of second choice—man.

Immunity.—An attack of plague usually brings about a state of permanent immunity. Both active and passive immunity may be produced by artificial means.

Laboratory Diagnosis.—The important methods of laboratory diagnosis are the agglutination test on the patient's blood serum, and the demonstration of the bacilli in the lesions by smears, cultures, and animal inoculation.

Specific Therapy.—Antiserums are often disappointing as a therapeutic agent but are of distinct benefit in some cases. Vaccines produce an immunity lasting about six months in

about 50 per cent of cases. Their injection is often followed by severe reactions and they should not be given unless there is a real danger of contracting the disease.

Prevention.—The prevention of plague depends on the eradication of rats and their fleas. It is especially important to prevent the transportation of rats from infected to noninfected localities by trains and ships. Patients with plague should be isolated in well-screened, vermin-free rooms. Although it is seldom that patients with bubonic or septicemic plague transmit the infection to others, no chance should be taken and they should be nursed with the same precaution and their excreta should be disposed of in the same manner, as in typhoid fever. The sputum from patients with pneumonic plague should receive special care. The room should be disinfected with sulphur dioxide, because this agent destroys vermin. Rat-infested ships should be fumigated with hydrocyanic acid gas. Persons attending patients with plague should protect themselves with plague vaccine.

IV. Tularemia

Tularemia (rabbit fever) is an acute infectious disease of wild animals, especially rodents, that is transferred from animal to animal by the bite of an insect. It may be transmitted from animal to man by the bite of an insect, but human infections are usually caused by contamination of the hands or conjunctiva by the tissues or body fluids of an infected animal or insect.

Pasteurella Tularensis.—*Pasteurella tularensis* derives its name from Tulare County, California, where the disease was first observed. It has some of the characteristics of both the *Brucella* and the hemorrhagic septicemia group of organisms, but it also has characteristics which separate it from both of them. *Past. tularensis* is a small, nonmotile organism, showing marked variation in size. It is gram-negative and does not form spores. It does not grow on ordinary media but grows on cystine agar. It can be easily demonstrated in the lesions of the disease by animal inoculation. It is the most easily communicable of all organisms, and practically every labo-

ratory worker who has investigated tularemia has contracted the disease. According to some workers, *Past. tularensis* is susceptible to the action of certain of the sulfonamide drugs.

Clinical Types of Tularemia.—Tularemia occurs in four clinical types, all of which are accompanied by most severe constitutional symptoms, such as pain, fever, and prostration. These types are: (1) the ulceroglandular, characterized by an ulcer at the site of infection with involvement of the regional lymph nodes, (2) the oculoglandular, which is the same as the ulceroglandular with the conjunctiva as the site of primary infection, (3) the glandular, in which the lymph nodes are involved but ulceration is absent, and (4) the typhoid type, in which neither ulceration nor lymph node involvement is present. Death occurs in about 5 per cent of cases. Those who recover are incapacitated for weeks or months.

Mode of Infection.—The animals in which tularemia is most prevalent are cottontail rabbits, jack rabbits, snowshoe rabbits, and ground squirrels. Certain birds have tularemia, and it is not unknown in sheep. Altogether, more than twenty species of wild animals are known to be infected. Tame rabbits are susceptible, but ordinarily they do not contract the disease because they do not harbor the small parasites which transmit the infection from animal to animal. The insects that transmit tularemia from animal to animal are wood ticks, rabbit ticks, lice, horseflies, and squirrel fleas.

In our country, at least, man usually contracts tularemia by handling infected rabbits and of these about 70 per cent are of the cottontail variety. Cold storage rabbits remain infectious for two or three weeks. The disease may be contracted by eating insufficiently cooked rabbit meat. Wood ticks, dog ticks, horseflies, and squirrel fleas may sometimes transmit the infection to man. Rabbit ticks, rabbit lice, and mouse lice which are important agents in transferring the disease from rodent to rodent do not bite man. In Russia human infections are often contracted from a species of fur-bearing water rat. The ocular type of tularemia is usually contracted

by rubbing the eye with contaminated fingers. Tularemia is not transmitted directly from man to man. Laboratory infections are rather common.

Laboratory Diagnosis.—The laboratory diagnosis of tularemia depends on the agglutination test, bacterial skin tests, and the inoculation of guinea pigs with material from the lesions. Smears and cultures are of little value, if any.



Fig. 92.—Ulcer formed at site of infection in tularemia. (From Stitt: *Diagnostics and Treatment of Tropical Diseases*. P. Blakiston's Son & Co.)

Immunity.—An attack is followed by a permanent immunity.

Specific Therapy.—Foshay's vaccine produces an immunity which lasts for about a year.

Prevention.—The nature of the infection and its mode of transfer render the preventive measures obvious.

V. Brucellosis (Undulant Fever)

Within the *Brucella* group are included three organisms which primarily attack lower animals, from which they are often transmitted to man. They are bacteriologically closely related. One, known as *Brucella melitensis*, produces Malta fever in goats and sheep, a disease characterized by prolonged fever, arthritis, and a tendency to abort. Another, known as *Brucella abortus*, causes contagious abortion, or Bang's disease, in cattle. The third, known as *Brucella suis*, causes contagious abortion in hogs. Contagious abortion of cattle and hogs is characterized by a tendency to abort, retention of placentas, sterility, and postpartum death of offspring. Infections in man are characterized by a long-continued fever, or cycles of fever alternating with afebrile periods, marked weakness, and a tendency toward profuse perspiration. Melitensis infections are common in the Mediterranean basin and in the southwestern United States. Infection was brought to the latter by goats imported from the former. *Br. abortus* and *Br. suis* infections are more widely spread, or at least such is the case in the United States. Various names have been applied to the disease in man, most common of which are Malta fever (on account of its prevalence on the Island of Malta), undulant fever (on account of its clinical course), brucellosis and brucelliasis. In Southwest Texas it is often spoken of as goat fever and Rio Grande fever.

General Characteristics of *Brucella*.—Organisms of the *Brucella* group are small, nonmotile, ovoid, gram-negative, nonspore-forming bacilli. They are so closely related to each other that they cannot be differentiated by agglutination tests or ordinary cultural methods. Special cultural methods seem to give differential characteristics. *Brucella* grow on all ordinary media but growth is slow. *Br. melitensis* and *Br. suis* grow under ordinary oxygen conditions. For the growth of some strains of *Br. abortus* the presence of from 5 to 10 per cent of CO₂ in the air is necessary. *Brucella* are destroyed within ten minutes by a temperature of 60° C. They will remain alive and virulent for as long as four months in dark, damp surroundings.

Pathogenicity.—*Brucella melitensis* is more pathogenic for man than *Br. suis* and the latter is more pathogenic than *Br. abortus*. With the exception of hogs which are infected with *Br. suis* only, animals may be infected with either type. *Brucella* are capable of attacking every organ and tissue of the body. For this reason a person with brucellosis may seek as his initial consultant internist, surgeon or any other specialist.

Source and Mode of Infection.—Infection is widespread among goats, cattle, and hogs. In cattle it ranks with tuberculosis as a source of economic loss. Human infections are common but often overlooked. Infection is transmitted from animal to animal by food contaminated with the urine or feces or lochia of infected animals or by contact with infected placentas or fetuses. Suckling animals may become infected by the milk of infected mothers. Man becomes infected by eating dairy products from infected cows or by handling infected material. Packing house workers and butchers often become infected by handling the meat of infected hogs. Farmers, stockmen, and veterinarians become infected by handling infected cows. Infection with *Br. melitensis* is contracted by drinking the unpasteurized milk of infected goats. In most cases the infectious material is derived from the excreta of living animals or the blood or tissues of dead animals and enters the body through cuts or abrasions of the skin. Infection is seldom if ever transmitted from man to man. Cows may become carriers and excrete the organisms in their milk for as long as seven years. Dust containing the organisms may cause infection.

Laboratory Diagnosis.—Laboratory aids in the diagnosis of undulant fever are blood cultures, agglutination tests, skin tests for sensitivity to *Brucella*, feces cultures, urine cultures and the opsonocytophagic test. The latter is a test to determine the ability of the leucocytes to phagocytose *Brucella*. Chief reliance is placed in the agglutination test. Many workers believe that by properly interpreting the results of the agglutination test, opsonocytophagic test and intradermal test for sensitivity to *Brucella* it can be correctly determined whether the patient is susceptible, infected or immune to undulant fever.

Immunity.—One attack probably confers a permanent immunity. Children under ten years of age seldom contract the disease. Men are more often attacked than women, but this is probably due to greater exposure.

Specific Therapy.—Vaccines seem to give good therapeutic results. Serum therapy is yet in the experimental stage.

Prevention.—All milk (including goat's milk) should be pasteurized. Infected animals should be removed from the herd. Although transfer from man to man seldom if ever occurs, the excreta of a patient with undulant fever should be disposed of in the same way as those from a case of typhoid fever.

VI. Glanders (Farcy)

Glanders is primarily a disease of horses, mules, and donkeys, which may sometimes be transmitted to man. Occasionally it occurs in lower animals other than the ones mentioned. It is caused by *Malleomyces mallei* and is characterized by the formation of tubercle-like nodules that undergo ulceration. They occur most often in the lungs, superficial lymph nodes and mucous membranes. When affecting the lymph nodes of animals it is known as *glanders*; when affecting the mucous membranes it is known as *farcy*. It is a highly contagious disease and was at one time very prevalent but, with the replacement of the horse by the automobile, has become an uncommon disease.

M. mallei is a narrow, sometimes slightly curved bacillus that is gram-negative and non-motile. It shows considerable variation in size. *M. mallei* is a most dangerous organism and material from the lesions and cultures should be handled with extreme care or the worker will become infected. All excreta of a diseased animal contain the bacilli.

The mode of transfer of the disease from animal to animal is not well understood. There is some evidence that infections occur by way of the lungs. Man is most often infected by coming in contact with the tissues or excreta of diseased animals. The organisms usually enter the body by a wound, scratch or abrasion of the skin. Laboratory workers may become infected by handling cultures.

The disease is diagnosed in man by isolating the bacilli from the lesions. *Mallein* is a product of *M. mallei* prepared in the same general way that tuberculin is prepared from *Myco. tuberculosis*. It is used in the diagnosis of the disease in animals. By its use many occult cases have been discovered.

The control of glanders depends on the destruction of animals that have the disease in its clinical or occult form and the disinfection of stables, blankets, harness and drinking troughs used by animals with the disease. In man prevention depends on avoiding infectious material.

VII. *Pseudomonas Pyocyanea*

Pseudomonas pyocyanea is an actively motile, gram-negative, non-spore-forming bacillus which, when stained with simple stains, bears some resemblance to *C. diphtheriae*. It is characterized by the diffusion of a blue pigment through the medium on which it is grown. The same color is seen in purulent discharges brought about by *Ps. pyocyanea*. The production of a green pigment is a characteristic of several species of bacteria, but the production of a blue pigment (pyocyanin) seems to be specifically identified with *Ps. pyocyanea*.

Ps. pyocyanea is a normal inhabitant of the skin and upper respiratory tract of man and animals. It is ordinarily only slightly pathogenic and causes primary infections only when the resistance of the host is lowered. It is often a secondary invader and frequently delays the repair of wounds. Among the diseases that may be due to *Ps. pyocyanea* are otitis media, abscesses, suppuration of wounds, infections of sinuses, and septicemia. All of these, however, are more often due to other organisms than to *Ps. pyocyanea*.

VIII. Bacilli of the *Proteus* Group

The proteus group is a group of motile organisms which are gram-negative, do not form spores, and are normal inhabitants of feces, water, and sewage. These organisms grow rapidly on ordinary media and are pathogenic for rabbits

and guinea pigs. Their primary pathogenicity is slight, but they are of considerable importance as secondary invaders. They are next to colon bacilli in importance as a cause of cystitis and pyelonephritis. They are on rare occasions the cause of peritonitis and endometritis.

It is a peculiar fact that, although proteus bacilli does not cause typhus fever or act as secondary invaders in cases of typhus, the blood serum of a patient with typhus fever will agglutinate certain strains of proteus bacilli. This is the basis of the Weil-Felix reaction for typhus fever.

IX. The Friedländer Bacilli

The Friedländer bacilli make up a group of organisms whose biological characteristics indicate that they are related to the colon bacilli while their disease-producing capacities indicate that they are related to the organisms causing respiratory infections. They are nonmotile, gram-negative, aerobic organisms that are surrounded by a broad well-developed capsule. They grow luxuriantly on ordinary culture media.

One of the group, which is the type organism of the group, is known as *Bacillus mucosus-capsulatus*, Friedländer's bacillus, or the pneumobacillus. It was discovered by Friedländer previous to the discovery of the pneumococcus and was thought by him to be the sole cause of pneumonia. It is now known that it is responsible for less than 10 per cent of cases. Pneumonia due to Friedländer's bacillus may be of either the lobar or lobular type and is characterized by its severity and high fatality. Middle ear infections and meningitis may occur as complications. Friedländer's bacillus is occasionally responsible for diseases other than pneumonia. One of these is septicemia.

Questions for Review

1. Discuss the proper disposal of the bodies of animals dead of anthrax.
2. Discuss the mode of infection in Asiatic cholera.
3. Discuss the prevention of plague.
4. How does man become infected with *Brucella*?
5. Name some diseases caused by *Ps. pyocyaneus*.
6. What is the basis of the Weil-Felix reaction for typhus fever?

True-False Test

Place the word "true" or "false" before each statement.

- 1. *B. anthracis* is the only spore-forming aerobic pathogenic bacterium.
- 2. *B. anthracis* was discovered recently.
- 3. It is not necessary to isolate patients with anthrax.
- 4. People may be immunized against anthrax.
- 5. Asiatic cholera is an infectious disease.
- 6. Permanent carriers of Asiatic cholera are frequently found.
- 7. An active immunity to Asiatic cholera may be established by vaccination.
- 8. The immunity following an attack of cholera is of long duration.
- 9. Plague bacilli may live outside the body in the carcasses of dead rats and in sputum for some time.
- 10. Plague bacilli produce an endotoxin.
- 11. Bubonic plague is transmitted to man by the bite of a flea that has previously fed on an infected rat or an infected person.
- 12. An attack of plague brings about an immunity of short duration.
- 13. The use of antiserums in treating plague may be of benefit.
- 14. The organisms causing tularemia are the most communicable of all organisms.
- 15. Tularemia may be transmitted from man to man.
- 16. One attack of undulant fever confers a permanent immunity.
- 17. Serum therapy for undulant fever is yet in the experimental stage.

Completion Test

- 1. Anthrax is an acute infectious disease caused by -----
- 2. Animals usually contract anthrax by way of the -----
- 3. Anthrax in man may be contracted by -----
- 4. Anthrax is also known as ----- due to the enlargement of the -----
- 5. *B. anthracis* leaves the body in the exudate of local lesions (-----) and in ----- and -----
- 6. Asiatic cholera affects the lower part of the -----
- 7. Two forms of plague are ----- and -----
- 8. Plague is due to the organism -----
- 9. ----- fever is another name for the acute infectious disease known as tularemia.

10. Tularemia is caused by *Past.* -----.
11. Four clinical types of tularemia are: (1)-----,
(2)-----, (3)-----,
(4)-----.
12. Tularemia may be transmitted to man -----,
-----, and -----.
13. What three organisms cause undulant fever in man?
 1. -----
 2. -----
 3. -----
14. What disease does each cause in lower animals?
 1. -----
 2. -----
 3. -----

References

- Zinsser and Bayne-Jones: Textbook of Bacteriology, New York, 1939,
D. Appleton-Century Co.
- Rosenau, Milton J.: Preventive Medicine and Hygiene, New York, 1935,
D. Appleton-Century Co.
- Stitt, E. R.: Diagnosis and Treatment of Tropical Diseases, Phila-
delphia, 1938, P. Blakiston's Son & Co.
- American Public Health Association: Undulant Fever, A Symposium.
- Huddleston, I. F.: Brucellosis in Man and Animals, New York, 1943,
Commonwealth Fund.
- Evans, Alice C.: Brucellosis in the United States, Am. J. Pub. Health
37: 139, 1947.
- Zinsser, Hans: Rats, Lice and History, Boston, 1935, Little, Brown &
Co.
- Smillie, Wilson G.: Preventive Medicine and Public Health, New
York, 1946, The Macmillan Company.

CHAPTER XXIX

DISEASES CAUSED BY FILTRABLE VIRUSES

Filtrable or ultramicroscopic viruses are agents that are capable of causing infectious diseases, usually cannot be seen with an ordinary microscope, can be propagated only in the presence of living tissues where they develop within the cells, and are capable of passing through filters that retain all ordinary bacteria. We know something about their action, but we do not know what they actually are because only a few have been prepared in a pure state and they are usually destroyed when they are separated from the cells which they attack. Cells that have been specifically attacked by filtrable virus often contain small round or oval bodies known as *inclusion bodies*. Some observers believe that filtrable viruses are organisms so small that we cannot see them and others believe that they are of the nature of enzymes. Their resistance to destructive influences is about the same as that of ordinary bacteria. They are resistant to the action of carbo-lic acid and may be preserved for months in glycerin. They probably are able to reproduce because after several days' cultivation in the presence of living tissues the concentration of the virus in the culture may increase thousands of times. Filtrable viruses are responsible for more than eighty diseases of plants, many diseases of the lower animals, and some of the most highly communicable and dangerous diseases of man. They attack practically all plants of commercial importance. Attacks of diseases caused by filtrable viruses are usually, but not always, followed by a strong and lasting immunity. Present evidence indicates that the majority of the virus diseases are not benefited by the sulfonamide drugs or the antibiotics.

The filtrable viruses may be classified into three classes; namely, (1) those whose characteristic lesions appear on the skin (smallpox, measles, chicken pox, etc.), (2) those characterized by catarrhal inflammations (common cold, influenza, etc.) and, (3) those which primarily affect the central nervous system (rabies, acute anterior poliomyelitis,

encephalitis, etc.). In the following pages only a few of the most important of these diseases affecting man will be discussed.

I. Smallpox (Variola)

Smallpox is a highly communicable disease that is characterized by severe constitutional symptoms and a rash that goes through a typical evolution. The incubation period is about 12 days. Man's ability to prevent disease is nowhere better exemplified than in smallpox, because before



Fig. 93.—Child with smallpox; vaccinated brother and sister. These children came to the Philadelphia General Hospital with their mother who had smallpox. The child in the middle had not been vaccinated. The other two had been vaccinated because it was required before attending school. (From Schamberg and Kolmer: *Acute Infectious Diseases*. Lea and Febiger.)

the days of vaccination smallpox spread over the world in great epidemics. It has been estimated that in some of these epidemics 95 per cent of the population were attacked and 25 per cent died. It seems strange that we yet allow smallpox to exist when it is completely within our power to eradicate it. Apparently there are two types of smallpox virus. One causes a rather severe form of the disease. Infections due to

the other type are characterized by extreme mildness. The type causing the more severe attacks of the disease is the most common.

Smallpox is transmitted directly from person to person by droplet infection or through the air in the vicinity of the patient. It may sometimes be conveyed by objects, such as handkerchiefs, pencils, etc., that have been contaminated with the nasal and buccal secretions of a person with smallpox. It may be transmitted from the pustules by the hands. Persons immune by virtue of vaccination or an attack of the disease may become contact carriers



Fig. 94.—Smallpox vaccination showing a “take.” (From Kolmer; *Infection, Immunity, and Biologic Therapy*. W. B. Saunders Co.)

and disseminate the disease for a short period. It is generally supposed that the infectious agent enters the body by the respiratory tract and leaves by the buccal and nasal secretions. The causative agent may be found in the blood, skin lesions, and secretions of the mouth and nose. The patient may infect others before the eruption appears and the period of infectivity extends long into convalescence. Even the dead body may be a source of infection. A mother with smallpox may infect her child in utero, and the child may be born with a typical smallpox eruption. Epidemics among

monkeys have occurred. Injected into calves or rabbits, the virus produces cowpox.

An attack of smallpox usually renders the patient immune for the remainder of his life. Edward Jenner, being familiar with the tradition current among the country people of England that after an attack of cowpox a person would not contract smallpox, laid the foundation for the modern method of vaccination against smallpox by transferring matter from a cowpox pustule on the hand of a dairymaid to the arm of a boy who was susceptible to smallpox. After this the boy was twice inoculated with smallpox without contracting the disease. These far-reaching experiments were performed in 1796. Smallpox vaccination as performed today consists of infecting the person with cowpox and the vaccine used is the purified material obtained from the skin lesion of calves with cowpox. There has been much discussion as to the relation of smallpox and cowpox. Many workers believe that they are distinct but closely related diseases, but the majority believe that they are due to the same virus and that the difference in manifestations depends on an adaptation of the virus to the cow and man respectively. It is also believed that cowpox originated by the transfer of smallpox from man to the cow. Whatever the relation may be, it remains true that inoculation with cowpox (vaccination) renders a person immune to smallpox, and as long as he is immune to smallpox he cannot be inoculated with cowpox; i.e., a vaccination will not "take."

A short sketch of the method of preparing smallpox vaccine was given on page 217.

Children should be vaccinated when they are six months old and again at the end of five or six years. All persons, including those who have had smallpox, should be vaccinated during an epidemic or when exposed. Vaccination during infancy has certain advantages. Among these are: (1) the "take" is likely to be milder, (2) it makes subsequent vaccinations milder, (3) the scar is less noticeable and (4) the child is protected in its early years.

An immunity sufficient to protect against smallpox usually develops within ten days after a primary vaccination and probably sooner after a secondary vaccination.* This immunity lasts a variable period. In some it lasts only a few years while in others it may protect for a lifetime. Vaccination cannot be repeated too often, because if a person is immune to smallpox the vaccination will not take. Failure of a vaccination to take in persons who are not immune to smallpox is most often due to faulty technic or inactive vaccine. It should be remembered that vaccine virus is very susceptible to even moderate warmth and should be kept on ice. Those who have been vaccinated seldom die of smallpox, even though they were vaccinated two or three decades before the attack.

When preparing the arm, alcohol, especially if medicated, should not be used because it destroys the virus. Following vaccination the following reactions may occur:

1. *Primary take*, which occurs in those who have no or little immunity. On the fourth day a small circumscribed solid elevation of the skin (papule) appears; on the seventh day the lesion contains fluid (vesicle) and has a pink areola around it. On the ninth day it is filled with pus (pustule), and it is dried up at the end of fourteen days.

2. *Accelerated reaction*, which occurs in those who are partially immune. The vesicle is present at the fifth day; it becomes a pustule about two days later, and the reaction is over at the end of ten days.

3. *Reaction of immunity*, in which a papule appears within two days and disappears within three days.

Smallpox is one of the most highly communicable diseases. Patients with smallpox should be isolated. The nurse should be isolated and of course vaccinated. All objects that come in contact with the patient should be sterilized, preferably by heat. If this cannot be done, they should be soaked in 1:1,000 bichloride solution. Carbolic

*Smallpox and rabies are the only diseases in which the exposed person can be protected against the development of the disease by the production of an active immunity. In smallpox an active immunity develops very quickly. In rabies the period of incubation is so long that an active immunity can be produced before the disease takes effect.

acid has little effect on smallpox virus. The feces and urine should be disinfected with chloride of lime. Sputum and discharges from the mouth and nose should be received on tissues and burned. The patient should not be released until desquamation is complete. Vaccination against smallpox should be a universal procedure.



Fig. 95.—Vaccination by the multiple pressure method. In this method a drop of vaccine is placed on the properly cleansed arm and the operator pulls the skin taut with one hand and with the other hand presses the side of a needle point through the drop of vaccine and firmly against the skin. The needle point is not pushed into the skin but with each pressure some of the vaccine is introduced into the skin. When properly done with the proper kind of virus, practically 100 per cent of takes will occur in nonimmune subjects.

II. Measles (Rubeola)

Measles is an acute communicable disease characterized by a catarrhal inflammation of the respiratory passages, fever and constitutional symptoms, a skin eruption, and a distinct tendency to develop grave complications. Among these are pneumonia, otitis media, mastoiditis, etc. It often fans a smouldering tuberculosis into activity. It is one of

the most common diseases and is said to be responsible for about 1 per cent of deaths occurring in the temperate zones. The incubation period is 10 or 11 days.

Many organisms, especially certain strains of streptococci, have been said to be the cause of measles, but it seems that the most convincing evidence is in favor of the etiological role of a filtrable virus. The causative agent is found in the blood, the secretions of the eyes, and the respiratory tract.

It is presumed that the virus of measles is thrown off from the body in the lacrimal, nasal, and buccal secretions and enters the body by the mouth and nose. The infection is usually transmitted directly from person to person. The infectious period of objects contaminated with the secretions of a patient with measles is of short duration. Measles is not transferred by the scales from the skin. Neither is the infection likely to be transmitted from the sick to the well by a third person. It may be spread a considerable distance through the air. Measles is most highly communicable during the three or four days preceding the eruption. It is not transmitted after the fever has subsided. Epidemics have a tendency to recur every two or three years and are likely to break out when young adults from rural communities come together in large groups, as occurs when armies are mobilized. The disease is especially virulent in primitive races.

Children of mothers who have had measles are immune to the disease until they are about six months old. This is due to antibodies transferred from the mother via the placenta. An attack usually produces a permanent immunity. Measles may be prevented or the severity lessened by the injection of measles antibody in the form of adult immune serum, convalescent serum, immune globulin, or gamma globulin. The difference in adult immune serum and convalescent serum is that the former is from a person who has had measles long ago and the latter is from a person recently recovered from the disease. Immune globulin is a protein material rich in antibodies extracted from human plascentas. Gamma globulin is a certain refined portion of blood plasma which is more than twenty times as rich in

antibodies as the plasma from which it was prepared. If sufficient antibody is injected within four days after exposure, measles is usually prevented. If given between the fifth and ninth day the disease is modified; i.e., its severity is lessened. After the rash and other symptoms have appeared, the administration of antibody has little effect. In many cases it is better to modify measles than to prevent it, because the immunity that prevents the disease is passive and of short duration, while that which follows the modified disease is active and permanent.

Measles has a depressive action on certain allergic conditions and immune processes. It renders the tuberculin and agglutination tests less positive or even negative. The Dick and Schick tests may become more strongly positive, and eczemas and asthmas often disappear during or after the attack.

Uncomplicated measles is not very dangerous, but measles seems to render the patient especially vulnerable to a streptococcus or pneumococcus bronchopneumonia. The patient should be isolated and protected against streptococcus infections, staphylococcus infections, common colds, and other depressing influences. Discharges from the nose, mouth, and eyes should be disinfected. When measles appears in army camps, etc., daily inspections of personnel should be made, and those having conjunctivitis, colds, or fever should be isolated. The liability of patients with measles to develop pneumonia should always be kept in mind, and the development of this complication should ever be guarded against.

III. German Measles

German measles is a mild but highly prevalent disease of virus origin which is important because it is often confused with other diseases and because children born of mothers who have German measles during pregnancy may have such defects as cataract or deaf-mutism.

The disease with which German measles is most often confused is scarlet fever. German measles is followed by a permanent immunity.

IV. Epidemic Parotitis (Mumps)

Mumps occurs most often between the fifth and fifteenth years. The causative agent is found in the saliva during the first six days of the disease and may be found in the blood stream of patients with marked constitutional symptoms. Blood stream transfer of the virus is responsible for such complications as orchitis, oophoritis, and pancreatitis. Mumps is usually transferred directly from person to person by droplets or saliva, but indirect transfer by contaminated hands or inanimate objects may occur. It may be possible that carriers play a part in its spread. The period of contagion begins before the glandular swelling and persists until after it has subsided. Convalescent serum given from seven to ten days after exposure protects a high proportion of children from infection. Adult epidemics may occur in military organizations and are extremely difficult to control. An attack of mumps is usually followed by a permanent immunity and, contrary to lay belief, the same immunity follows a unilateral involvement as a bilateral one.

V. Influenza

Influenza is a highly communicable disease which usually occurs in epidemics that are characterized by an explosive onset, a rapid spread, an involvement of a high percentage of the population, and frequency of serious secondary bronchopneumonia. It is estimated that in the pandemic of 1918-1919 there were 200,000,000 cases and 10,000,000 deaths from influenza. In the United States alone there were 500,000 deaths.

It was formerly thought that *H. influenzae* was the cause of influenza, but it is now known that it is caused by a filtrable virus or viruses. *H. influenzae* is of importance, however, on account of being a secondary invader in this disease and other respiratory infections. The disease has been produced artificially in chimpanzees, ferrets, and mice by injection of filtrates of nose and throat washings from known cases. At least two different strains of the virus known as A and B have been isolated. There may be other strains. According to some observers, the pandemic of

1918-1919 was due to virus A; according to others, it was caused by a virus which was neither A nor B.

The infectious agent in influenza enters the body by the mouth and nose and leaves the body by the same route. The disease is probably spread by indirect contact, direct contact, and droplet infection. An epidemic is usually of short duration and quickly subsides to be followed after several weeks (most often thirty-three) by a secondary wave, a free period, and a tertiary wave. In no cases does the infection spread faster than people travel. The explosive outbreak of an epidemic may be explained by the high communicability of the disease, the great number of susceptible people, and the fact that during the early days of the attack the patient is not confined to bed but mingles freely with other people. The average duration of an epidemic in a community is from six to eight weeks.

In secondary and tertiary outbreaks the number of people attacked is less than in a primary outbreak, but the disease is more severe, complications are more common, and the mortality is higher. Fortunately they travel slower and do not spread as widely as primary outbreaks. Interepidemic cases are usually comparatively mild. There seems to be an etiological relation between influenza and encephalitis because an epidemic of the former is often followed by an increase in the number of cases of the latter.

A considerable portion of the population apparently possesses some degree of natural immunity to influenza because during an epidemic from 25 to 75 per cent of the population escape infection. After an attack of the disease some degree of immunity persists for probably a few weeks or months, but second and third attacks have been known to occur in rapid succession. The production of an active immunity by influenza virus vaccine (see page 219) has met with considerable success. Little success has been obtained in producing a passive immunity by means of convalescent serum or immune serum.

When an epidemic of influenza strikes, all the methods known to preventive medicine fail to hold it in check. Wholesale isolation seems to be of little value. Masks seem to be

of little help. Nurses attending cases of influenza should disinfect the mouth and nasal secretions of the patient and should avoid exposing themselves to droplet infection. The patient should be kept in strict isolation.

Swine Influenza.—Swine influenza is a severe respiratory infection of hogs caused by the combined action of a filtrable virus and a bacterium. The bacterium is closely related to *B. influenzae*, and the virus is closely related to the virus of human influenza. The diseases differ in that the human virus can produce the complete disease, while the virus of swine influenza alone produces only a mild form of the disease.

VI. The Common Cold

The common cold temporarily disables more people than any other infectious disease and is of danger to life because it lowers vitality and is often complicated or followed by such diseases as pneumonia and influenza and such streptococcus infections as endocarditis and rheumatic fever. Factors that predispose to colds are exposure to chilling and dampness, sudden changes in temperature, dusty atmospheres, drafts, loss of sleep, overwork, and lowering of general body vitality.

Colds are spread most often by direct contact. Not only does the affected person spread his cold to others, but, because of coughing and sneezing, he is more likely to spread bacteria which he may be carrying. Colds are most communicable in their early stages.

Some people are comparatively resistant to colds, while others are comparatively susceptible and have cold after cold. A general lowering of body resistance seems to increase susceptibility, but the most hardy are often attacked.

The general public should be made cognizant of the danger of colds and the serious diseases that accompany or follow them. Contact with people having colds should be avoided. Children with colds should be kept out of school. If people will go to bed as soon as they feel a cold coming on, many cases will be avoided, because the patient thus isolates himself at the time when the infection is most likely to be transmitted to others. Promiscuous kissing of children should be

looked upon with disfavor, and antispitting ordinances should be strictly enforced. The patient should make it his business to see that the secretions from his mouth and nose do not come in contact with others. Those who care for the sick should use every precaution against contracting colds. Disinfection of the nose and throat with argyrol solution (20 per cent) seems to have some preventive value. Vaccines have not been universally accorded any great prophylactic importance.

VII. Poliomyelitis (Infantile Paralysis)

Although poliomyelitis was first observed more than eighty years ago, we must yet confess lack of knowledge or complete ignorance of how it spreads from person to person, how it enters the body, and why epidemics start. It is an acute infectious disease which affects the brain, spinal cord, and certain nerves and may cause such destruction of nerve tissue that it is followed by a distinct train of symptoms referable to the central nervous system. It occurs in three forms: (1) abortive, in which all symptoms referable to the nervous system are absent, (2) nonparalytic, in which symptoms are referable to the nervous system, but no paralysis occurs, and (3) paralytic, in which paralysis occurs. Infantile paralysis is not a good name for the disease because it may occur in adults and paralysis is absent in many cases. In recent years the number of adult cases has increased.

Poliomyelitis may occur sporadically but has a tendency to occur in epidemics. The causative agent is found in the tonsils, lymph nodes, nose, throat, and feces. It has not been found in the blood. It can probably survive outside the body for some time. The mode of transfer is clouded in uncertainty. Early evidence indicated that the disease is conveyed by the secretions of the mucous membranes of the upper respiratory tract. This leads to the possibility of transfer directly from acute cases, abortive cases, and carriers. Other evidence suggests that it is contracted through the gastrointestinal tract. The finding of large amounts of the virus in the feces of patients and in sewage suggests that the infection might be transmitted by water, milk, or food. Insect vectors have been suggested. Con-

siderable evidence indicates that the usual portal of entry is the upper respiratory tract, especially the nasal mucosa. Whether it is contracted through the gastrointestinal tract is not known. In epidemics cases show little relation to each other or to a common source of infection. When a case occurs in a household, the other members are seldom affected.



Fig. 96.—Child with poliomyelitis. Note the position of the right foot. (From Zahorsky and Zahorsky. *Synopsis of Pediatrics*. The C. V. Mosby Co.)

Patients may remain carriers of the virus for a considerable time. There have been a few cases of congenital poliomyelitis in which the mother has the disease in the latter part of pregnancy.

An attack confers a lasting immunity, and a high percentage of adults have virus-neutralizing substances in their

blood. Infants inherit an immunity from their mother by placental transfer. Convalescent serum is of value in preventing the disease after exposure but is of little value in treating active cases. The patient should be isolated and the stools and fomites should be properly disinfected. Contacts, especially between children, should be reduced to a minimum during epidemics.

VIII. Epidemic Encephalitis

Epidemic encephalitis is an infectious disease that causes a diffuse degeneration of the central nervous system. It occurs in two major types, namely: type A which followed the influenza epidemic of 1918-1919, and type B to which belong the Japanese encephalitis of 1924, the St. Louis encephalitis of 1933, Russian encephalitis, and the various types of equine encephalomyelitis.

Epidemic encephalitis is probably an old disease, but it did not become prominent in modern medicine until 1917. Type A, which made its appearance at that time, was known as lethargic encephalitis or sleeping sickness. The term lethargic cannot be applied to all types of encephalitis because some cases are accompanied by excitement instead of lethargy. The term sleeping sickness is, of course, unsatisfactory because it has already been applied to another disease (African sleeping sickness caused by *Trypanosoma gambiense* and *rhodesiense*).

Although a virus has not been isolated in all types, it is assumed that epidemic encephalitis is due to a filtrable virus which has a special affinity for the central nervous system and that the infectious agent, transmitted by droplets of nasal and buccal secretion, gains access to the central nervous system by way of the nasopharynx.

The disease may occur sporadically or in epidemic form. The incidence among doctors and nurses is high and institutional outbreaks may occur. Peculiarly the members of a family in which a case occurs are not especially likely to contract the disease. That some cases of encephalitis may be due to the virus of equine encephalomyelitis is proved by the fact that in the last few years cases of human en-

cephalitis have followed epidemics of equine encephalomyelitis and that the virus of equine encephalomyelitis has been isolated from the central nervous system of some of these human cases. Present evidence indicates that equine encephalomyelitis is not transmitted directly from horse to man, but to man from some bird which harbors the virus. At least one species of wood tick and one species of mosquito are capable of transferring the infection. There may be other modes of transmission.

Encephalitis may follow measles, smallpox, smallpox vaccination and immunization against rabies. In the encephalitis following smallpox vaccination (postvaccinal encephalitis), most cases occur in children and young adults who have not been vaccinated before. Infants seem to be immune. Theories offered to explain postvaccinal encephalitis are: (1) it is a manifestation of vaccinia, (2) vaccination activates some latent virus in the body, and (3) the vaccine is contaminated with an encephalitis producing virus. The incidence of postvaccinal encephalitis is less than one case in 33,000 vaccinations. Vaccines to prevent the St. Louis and Japanese types of encephalitis are yet in the experimental stage. Their results are promising, however. Vaccines against the different types of virus have been prepared by growing the virus in chick embryos and treating it with formaldehyde. The one against the equine type has been used with a fair degree of success. A fairly effective antiserum has been prepared against this type of encephalitis. Encephalitis will be further discussed on page 631.

IX. Rabies (Hydrophobia)

Rabies is an acute, paralytic, uniformly fatal, infectious disease of warm-blooded animals including man. It is primarily a disease of the lower animals, and dogs are chiefly responsible for its propagation in civilized communities. Other domestic animals that contract rabies are cats, horses, cows, sheep, goats, and hogs. Wild animals that often contract it are wolves, foxes, skunks, and hyenas. All warm-blooded animals are susceptible. No instance of the transmission of the disease from man to man has been recorded.

Rabies occurs in two forms, the furious and the dumb. In the former, a stage of increasing excitability is followed by a stage of paralysis ending in death. In the latter, paralysis and death supervene without a preceding stage of excitement.

The rabies-producing virus is found in the nerve tissues and saliva of infected animals. It is transmitted by the saliva of rabid animals and is introduced into the body through a wound which is usually made by the bite of the animal conveying the infection. If a wound, such as a cut or abrasion, becomes accidentally contaminated with the saliva of a rabid animal, infection is as likely to occur as if the animal had inflicted the wound. Rabid animals are capable of transmitting the infection to others several days before they develop symptoms. When a person or animal becomes infected, the infectious agent passes from the site of inoculation along the nerve trunks to the central nervous system. When the brain is reached, the symptoms of rabies appear. Only about 25 per cent of people and 50 per cent of dogs bitten by rabid animals become infected.

The period of incubation of rabies is remarkable on account of its length. In man it varies from three to eight weeks with an average of forty days. In dogs it varies from eight days to a year with an average of from two to eight weeks. The nearer the site of inoculation to the brain, the shorter the period of incubation. It is also shorter in children than in adults.

Negri discovered certain bodies, known as Negri bodies, in the brain cells of animals with rabies. These bodies are found in almost 100 per cent of cases when the disease is fully developed and it is by finding them that the laboratory diagnosis of rabies is made. They are often absent during the early days of the disease. They were formerly thought to be protozoa and the cause of rabies. Most observers now believe that they are not protozoa but reactive or degenerative structures brought about by the presence of the rabies virus.

If a person is bitten by an animal suspected of having rabies, the animal should not be killed but should be placed

in the hands of a competent veterinarian for observation. If the animal has rabies, the symptoms will be sufficiently developed within one or two days for a definite diagnosis to be made. If the dog is well ten days after biting a person, the person is in no danger from the bite. If, on the other hand, the animal is destroyed at once, examination of the brain may fail to show Negri bodies because they are often absent in the early stages of the disease.

The nursing precautions in rabies are rather simple. All that is necessary is to sterilize the secretions from the mouth and nose of the patient and articles contaminated with them. If laws, such as muzzling of dogs and making owners liable for the acts of their dogs, were rigidly enforced, rabies would soon disappear from civilized communities. There is an effective single-dose method of vaccinating dogs to prevent rabies. The immunity lasts about a year.

X. Yellow Fever

Yellow fever is an acute infectious disease characterized by an abrupt onset, a rapid course, and a high mortality. The most characteristic body change caused by the disease is a rapid and extensive destruction of liver tissue. Prominent symptoms are jaundice, albumin in the urine, hemorrhage, and vomiting.

Whenever yellow fever is discussed, eight names are brought to mind: Carlos J. Finlay, who first accused the mosquito of spreading yellow fever; Walter Reed, James Carroll, Jesse W. Lazear, and Aristide Agramonte, who, in 1900, formed the Commission of the United States Army to study yellow fever in Cuba; Privates John J. Kissinger and John J. Moran, who permitted themselves to be inoculated with yellow fever; and W. C. Gorgas, who applied the knowledge obtained to make the tropics more habitable for man. The members of the commission went to Cuba, lived in the tents of those who had had yellow fever, wore their clothes, and were bitten by infected mosquitoes. Carroll and Lazear contracted the disease, Lazear died. Kissinger and Moran were inoculated and refused any monetary reward. To these

men, all who live in tropical and temperate zones owe a debt of gratitude. The work of Gorgas is a fine example of the practical application of knowledge experimentally gained.

The virus of yellow fever is transmitted by the mosquito *Aedes aegypti*, which also transmits dengue fever. The mosquito bites a person during the first few days of illness and becomes infected. The virus multiplies in the body of the mosquito and reaches the salivary glands at the end of about twelve days; the mosquito remains infectious the remainder of her life. Only the female transmits the disease. When a nonimmune person is bitten by an infected mosquito, symptoms of yellow fever develop in from three to five days. The virus is found in the blood during the first three days of the disease.

Yellow fever yet remains endemic in many parts of the world, and we must always be on guard against it because the starting of an epidemic requires but three things: a person ill of the disease, mosquitoes to be infected, and people to be infected by the mosquitoes. The transport of infected mosquitoes by airplanes and other modes of travel is to be guarded against.

A source of yellow fever to be kept in mind is known as "jungle yellow fever." This is a type that occurs in lower animals, probably monkeys, and is transmitted by some insects, other than *Aedes aegypti*, from animal to animal and from animal to man. The virus seems to differ in no respect from that producing ordinary yellow fever. If man becomes infected, the infection is transmitted from him by *Aedes aegypti*.

A highly effective yellow fever vaccine has been prepared (see page 219). An immunity which lasts for about four years is established within four days after taking this vaccine. The value of convalescent serum is undetermined.

XI. Dengue Fever

Dengue, or "break bone" fever, is an acute disease which lasts about ten days and is characterized by a paroxysmal fever, intense joint pain, and mental depression. It is caused by a virus which is found in the blood during the early days

of the attack and is transmitted by the *Aedes aegypti* mosquito which, when once infected by biting a patient, remains infected the rest of her life.

When dengue fever is introduced into a community, a high percentage of the population contracts the disease. An attack of the disease is followed by an immunity which may persist for a year or two or the remainder of the patient's life.

XII. Infectious Hepatitis—Homologous Serum Jaundice

These diseases, which have a close resemblance to each other in certain respects and differ greatly in other respects, are thought to be of viral origin. How infectious hepatitis is contracted is not known. The virus is thought by some to enter the body by way of the mouth and to leave by way of the feces. Homologous serum jaundice is carried by human serum and may follow the use of convalescent serum, transfusion of blood, or the administration of vaccines, such as one type of yellow fever vaccine, which contain human serum. The fact that homologous serum jaundice may occur should be kept in mind when any of these procedures are carried out. Some workers believe that homologous serum jaundice is infectious jaundice artificially produced. The exact relation, if any, which exists between them is yet to be determined. Both are accompaniments of war and were especially prevalent during World War II. These conditions are further discussed on pages 677 and 681.

XIII. Venereal Lymphogranuloma

Venereal lymphogranuloma, or lymphogranuloma inguinale, formerly known as climatic bubo, is a venereal disease of virus etiology. It seems to be increasing in this country as well as all over the world. It should not be confused with granuloma inguinale which is also a venereal disease but is caused by a different etiological agent. Lymphogranuloma inguinale is detected from the laboratory standpoint by the Frei test which consists of the intradermal injection of material prepared from the suppurating buboes of patients or from

lymphogranulomatous mouse brains. The development of a bright red papule at the site of inoculation constitutes a positive test. The disease responds to certain of the sulfonamide drugs.

XIV. Virus Pneumonia

Virus pneumonia begins gradually as an upper respiratory infection and passes down to the lungs. The symptoms are fairly severe. The cough is paroxysmal but little sputum is raised. Only a single lobe of the lung may be involved. Complete consolidation is seldom present. The attack lasts several days or weeks. Fall of temperature and recovery are gradual. Epidemics among newborn infants have been reported. The disease is known also as primary atypical pneumonia.

XV. Other Diseases Caused by Filtrable Viruses.

German measles	Herpes zoster
Chickenpox	Molluscum contagiosum
Rift Valley fever	Herpes febrilis
Psittacosis	Foot and mouth disease
Canine distemper	Hog cholera

Questions for Review

1. Give the advantages of vaccinating children during infancy.
2. Discuss the prevention of smallpox.
3. Discuss the nursing precautions in smallpox.
4. Discuss the serum therapy of measles.
5. What are the nursing precautions in measles?
6. Discuss the nursing precautions in influenza.
7. Discuss the source of infection and mode of transfer of the infectious agent in poliomyelitis.
8. Discuss the mode of transmission of encephalitis.
9. Discuss the source of infection and mode of transfer of the rabies-producing virus.
10. Outline a logical mode of procedure to be followed when a person is bitten by an animal suspected of having rabies.
11. Discuss the source and mode of transfer of the yellow fever-producing virus.
12. Briefly discuss infectious hepatitis and homologous serum jaundice.

True-False Test

Place the word "true" or "false" before each statement.

- 1. Ultramicroscopic viruses are capable of passing through filters that retain all ordinary bacteria.
- 2. Filtrable viruses have been prepared in a pure state.
- 3. The incubation period of smallpox (variola) is twenty-one days.
- 4. An attack of smallpox usually renders the patient immune for the remainder of his life.
- 5. Edward Jenner laid the foundation for the modern method of vaccination in 1796.
- 6. Measles is most highly communicable during the last stages.
- 7. Uncomplicated measles is not very dangerous.
- 8. Convalescent serum given from seven to ten days after exposure to measles is of no value to children.
- 9. Patients may remain carriers of poliomyelitis for a considerable time.
- 10. All warm-blooded animals are susceptible to rabies.
- 11. A rabid animal cannot transmit the infection before it exhibits the symptoms of rabies.
- 12. The incubation period of rabies is longer when the person is bitten on the face.
- 13. The presence of Negri bodies in the brain of rabid animals is of little diagnostic importance.
- 14. An effective vaccine against yellow fever has been prepared.
- 15. A permanent immunity develops following an attack of dengue fever.
- 16. A filtrable virus may cause pneumonia.
- 17. The common cold temporarily disables more people than any other infectious disease.
- 18. Colds are most often communicable in their last stages.
- 19. Vaccines for colds are of great prophylactic importance.
- 20. If a mother has German measles during pregnancy, a defective child may be born.

Completion Test

1. Filtrable viruses may be classified into three classes:

1. -----
2. -----
3. -----

2. Smallpox is transmitted by ----- contact.
3. Smallpox may be conveyed by objects that have been contaminated with secretions from ----- and -----.
4. Epidemic parotitis may be transferred directly from person to person by ----- and indirectly transferred by -----.

5. Such complications as _____, _____, and _____ may accompany mumps.
6. Influenza is caused by a _____.
7. Influenza is probably spread by _____, _____, and _____.
8. There seems to be an etiological relation between influenza and _____.
9. Poliomyelitis occurs in three forms: _____, _____, and _____.
10. Epidemic encephalitis is a disease of _____.
11. Encephalitis may follow _____, _____, _____, and _____.
12. Two forms of rabies are _____ and _____.
13. The virus of yellow fever is transmitted by the mosquito _____, which also transmits dengue fever.
14. The common cold is often complicated by such diseases as _____, _____, and _____.
15. Colds are spread most often by _____-contact.

References

- Rosenau, Milton J.: *Preventive Medicine and Hygiene*, New York, 1935, D. Appleton-Century Co.
- Boyd, Mark F.: *Preventive Medicine*, Philadelphia, 1945, W. B. Saunders Co.
- Report of the International Committee for the Study of Infantile Paralysis, William Wood & Co.
- D'aunoy and von Haam: Venereal Lymphogranuloma, *Arch. Pathology*, 29: 1032 (June), 1939.
- Jordan and Burrows: *Textbook of Bacteriology*, Philadelphia, 1945, W. B. Saunders Co.
- Sulkin and Harford: The Laboratory Diagnosis of Virus Diseases, *J. A. M. A.* 122: 643 (July 3), 1943.
- Smillie, Wilson G.: *Preventive Medicine and Public Health*, New York, 1946, The Macmillan Company.
- Chant, Harry L.: Rabies, *Am. J. Nursing* 47: 390 (June), 1947.

CHAPTER XXX

BACTERIOPHAGE

In 1917 d'Herelle discovered that a bacteria-free filtrate obtained from the stools of bacillary dysentery patients contained a substance which, when added to a liquid culture of dysentery bacilli, caused the bacilli to dissolve. If a minute portion of the dissolved culture was added to another culture of dysentery bacilli the bacteria in this culture likewise dissolved. This transfer from culture to culture could be kept up until the bacteria in hundreds of cultures were dissolved, proving that the substance was not used up in the process but apparently increased in amount. He called this substance *bacteriophage* which means "bacteria eater."

Since that time bacteriophages against many bacteria have been isolated from many sources. The most plentiful sources, however, are the intestinal discharges of man or the higher animals and water or other materials contaminated with these discharges. Bacteriophages seem to be more plentiful in the discharges of those convalescent from infectious diseases. Some observers believe that they play an important part in recovery. Bacteriophages have been prepared against many organisms, but they have been most thoroughly studied in connection with the colon-typhoid group of organisms.

Several theories as to the nature of bacteriophages have been offered: namely, (1) that they are infinitesimally small microbes parasitic on ordinary bacteria, (2) that they are ferments, (3) that they are viruses attacking bacteria, and (4) that they are lifeless substances. It was formerly thought that all bacteriophage action was due to a single bacteriophage, but it is now believed that there are many bacteriophages and each one acts on its particular species of bacteria or group of species.

Bacteriophage has been used by local application, subcutaneous and intravenous injection in a number of pathological conditions, particularly in septicemia, infectious diseases,

and infections of the bladder and kidneys. As a whole the results have not been overly convincing and in some cases its use seems to be actually dangerous.

Questions for Review

1. What are some of the theories concerning the nature of bacteriophage?
2. Are there many bacteriophages or only one?

References

- Kolmer, John A.: The Nature and Therapeutic Applications of Bacteriophage, *Bull. Am. Soc. Laboratory Technicians* 1: 120 (July), 1935.
- Madison, R. R.: *Proc. Soc. Exper. Biol. and Med.* 38: 129 (Feb.), 1938.
- Fraser, Frieda H., and Madison, R. R.: *Proc. Soc. Exper. Biol. and Med.* 33: 307 (Nov.), 1935.

CHAPTER XXXI

DISEASES CAUSED BY RICKETTSIAE

Rickettsiae are small bacillary or diplobacillary bodies that stain with difficulty and cannot be grown on ordinary culture media. The pathogenic forms grow only in the cells of infected animals. Some grow in the cytoplasm; others grow in the nuclei of the infected cells. They grow well in the chick embryo and tissue cultures. Some observers believe that the *Rickettsiae* are inanimate objects but the majority agree that they are living microorganisms. Apparently they lie between the true bacteria and the filtrable viruses. So far as is known, they are little affected by the sulfonamide or antibiotic drugs. The *Rickettsial* diseases are transmitted to man by insects and give a positive Weil-Felix reaction. The Weil-Felix reaction is an agglutination test similar to the Widal test for typhoid fever except that the suspected blood serum is mixed with proteus bacilli instead of typhoid bacilli. This is a heterophile antibody reaction. *Proteus* bacilli do not cause any of the *Rickettsial* diseases or act as secondary invaders. *Rickettsiae* were named in honor of Dr. Howard T. Ricketts, who lost his life in their investigation.

I. Typhus Fever

Typhus fever is caused by *Rickettsia prowazeki*. It occurs in two rather distinct forms, Old World typhus and New World typhus. The former occurs in devastating epidemics. The latter occurs sporadically. For this reason Old World typhus is often spoken of as epidemic typhus and the New World typhus is often spoken of as endemic typhus. The New World typhus is endemic in Mexico and the southern United States. Mexican typhus fever is known as tabardillo. Brill's disease, which occurs along the Atlantic Coast, seems to be a mild form of Old World typhus. The attack of epidemic typhus is much more severe than that of the endemic type.

It is fairly well proved that in the New World there is a reservoir of infection in rats and that the infection is trans-

mitted from rat to rat by the rat louse and the rat flea. It is transmitted from rat to man by the rat flea and from man to man by lice. The reason epidemics do not occur in the Southern States as in Mexico and the Old World is most likely due to the absence of a heavy louse population. In the Old World an animal reservoir probably exists, but it has not been discovered. The louse that is usually responsible for the transfer of typhus from man to man is the body louse, but head lice are not incapable of transmitting it. It has not been determined whether lice and fleas transmit the infection by their mouths while biting or by contaminating the skin with their feces.

Typhus fever in its epidemic form is a disease of lice, poverty, filth, and overcrowding. It follows in the wake of famine, pestilence, and war. These conditions have little if anything to do with sporadic cases. An attack of typhus fever is followed by considerable immunity, but it is not always permanent. An active immunity has been brought about by vaccination. The vaccine is prepared by growing the Rickettsiae in lice, the chick embryo, mouse brain, or rat lung. In the sporadic typhus fever of the Southern States the mortality ranges from 2 to 4 per cent. The mortality in the epidemic form ranges from 10 to 20 per cent.

II. Rocky Mountain Spotted Fever

Rocky Mountain spotted fever is an infectious disease that bears a close resemblance to typhus fever and is caused by a similar organism of the genus, *Rickettsia*. In areas where it is well known it is often referred to as "tick fever." This should not cause it to be confused with relapsing fever, which also is known as "tick fever." It occurs chiefly in the Rocky Mountain states and the great majority of cases are found in Idaho and Montana. It occurs also on the Atlantic seaboard chiefly east of the Appalachian Mountains. For this reason two types of the disease are spoken of—the western type, which is the original Rocky Mountain spotted fever, and the eastern type seen along the Atlantic seaboard. The difference rests mainly on geographical distribution and mode of spread. It is a peculiar fact that while the mortality of the Idaho

variety of Rocky Mountain spotted fever is about 10 per cent, the mortality in the Montana variety reaches the alarming figure of 90 per cent.

The western variety is transmitted by the wood tick, and the eastern variety is transmitted by the dog tick. The female tick is able to transmit the infection to her offspring, and the male is capable of infecting the female. The tick is, therefore, able to maintain the disease in nature without either animal or human help. An attack renders a person immune for life. At the Rocky Mountain spotted fever laboratory at Hamilton, Montana, the disease is intensively studied and vaccines for its prevention are prepared. The vaccines are prepared by growing the *Rickettsiae* in chicken embryos.

III. Trench Fever

Trench fever is a remittent or relapsing fever that affects soldiers on trench duty but may occur in civil life when people live under conditions comparable to those of the trenches. It is thought by some workers to be caused by *Rickettsia pediculi* and to be transmitted by the body louse. Other workers now believe that it is caused by a filtrable virus. While trench fever is never fatal and recovery is usually complete, it may recur, and in some cases it is followed by a state of chronic ill health with pain in the limbs, mental depression, and impaired heart action. An attack does not confer immunity.

IV. Other Diseases Caused by *Rickettsiae*

Tsutsugamushi fever of Japan

Scrub typhus of Malaya

Bullis fever—First described at Camp Bullis, Texas

South African tick fever

“Q” fever

Typhus of India

True-False Test

Place the word “true” or “false” before each statement.

- 1. Some observers believe that the *Rickettsiae* are inanimate objects, but the majority agree that they are living microorganisms.

- 2. The attack of epidemic typhus fever is much more severe than that of the endemic type.
- 3. The immunity following an attack of typhus fever is not always permanent.
- 4. An active immunity to typhus fever has been brought about by vaccination.
- 5. The western type of Rocky Mountain spotted fever is transmitted by the dog tick.
- 6. There is a vaccine for the prevention of Rocky Mountain spotted fever.
- 7. It is now believed that trench fever is caused by a filtrable virus.

Completion Test

- 1. Two common diseases caused by Rickettsiae are ----- and -----.
- 2. The Rickettsial diseases are transmitted to man by ----- and give a positive ----- reaction.

References

- Zinsser and Bayne-Jones: Textbook of Bacteriology, New York, 1939, D. Appleton-Century Co.
- Zinsser, Hans: Rats, Lice and History, Boston, 1935, Little, Brown & Co.
- Baker, George E.: Rocky Mountain Spotted Fever, J. A. M. A. 122: 841 (July 23), 1943.
- Dyer, R. E.: The Rickettsial Diseases, J. A. M. A. 124: 1165 (April 22), 1944.
- Smillie, Wilson G.: Preventive Medicine and Public Health, New York, 1946, The Macmillan Company.
- Bayne-Jones, S.: Typhus, Am. J. Nursing 44: 821, 1944.

CHAPTER XXXII

SPIROCHETES AND ALLIED ORGANISMS

Spirochetes are actively motile, flexible, corkscrew-shaped organisms which may be found in water, soil, decaying organic matter, and in the bodies of animals or man. They move in a rotating sinuous manner but, with the exception of one species, do not have flagella. They have characteristics of both bacteria and protozoa, but most microbiologists consider them to be more closely related to the bacteria. They differ from bacteria in that within the body they are extremely susceptible to such drugs as arsenic, antimony, mercury, and bismuth. Spirochetes associated with the body of man may be nonpathogenic or pathogenic. Among those that are nonpathogenic are the spirochetes often found about the teeth and genitalia. Among those that are pathogenic are the spirochetes responsible for syphilis, yaws, relapsing fever, etc. Spirochetes have been variously classified as *Treponema*, *Leptospira*, etc.

I. Syphilis

Syphilis is a specific infectious disease due to *Treponema pallidum*. It may be contracted by inoculation (acquired syphilis) or by transmission through the placenta (congenital syphilis).

Treponema Pallidum.—*Treponema pallidum* (the pale treponema) is an actively motile, slender, corkscrew-like organism which, when properly searched for, can be found in practically every syphilitic lesion. It is especially abundant in chancres and mucous patches. *Treponema pallidum* is very difficult to stain and is best demonstrated in syphilitic lesions, such as chancres and mucous patches, by means of the dark-field microscope. Since the organisms are examined in the living state by this method, their two most important diagnostic features, motility and shape, may be observed. It is a highly invasive organism; that is, when introduced into the body through a local lesion it multiplies rapidly and quickly spreads over the body via the lymphatics and blood stream.

Treponema pallidum is capable of living outside the body under suitable conditions for a period of from ten to twelve hours but is killed within an hour by drying. It does not occur outside the body except on objects which have been contaminated with syphilitic secretions. It is susceptible to the action of penicillin, arsenic, and bismuth compounds. This organism was discovered by Schaudinn in 1905.

Under natural conditions *Treponema pallidum* infects man only, but monkeys, rabbits, and guinea pigs may be infected by artificial means. The origin of syphilis has been a subject of much debate. According to many students of the history of syphilis it was carried to Europe by sailors returning with Columbus from the New World. The disease seems to have spread over Europe in a severe epidemic at that time.

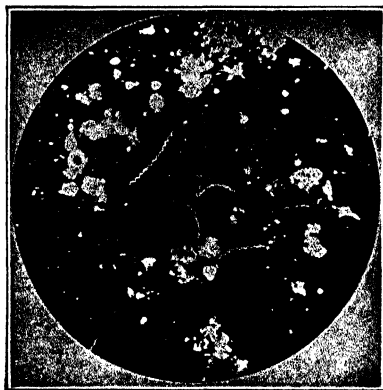


Fig. 97.—Dark-field illumination, showing *Treponema pallidum*. (Courtesy of The E. Leitz Co.)

Acquired Syphilis, Mode of Infection.—Acquired syphilis is most often contracted by direct contact, usually through sexual intercourse. The infection may be transmitted by kissing; this is especially true if the patient has lesions in his mouth. It is occasionally spread by contaminated objects, such as drinking cups, towels, etc. Physicians and nurses may become infected while examining a syphilitic patient. Blood and semen may sometimes convey the organism.

Evolution of a Typical Case.—As a rule, the first sign to appear after a person acquires syphilis is a sore which develops at the site of infection. This sore is known as a *chancre* or initial lesion. Briefly the evolution of a typical case of syphilis may be outlined as follows:

1. Infection occurs and the organisms spread throughout the body.
2. A chancre appears at the site of infection.
3. The chancre develops, ulcerates, and heals.

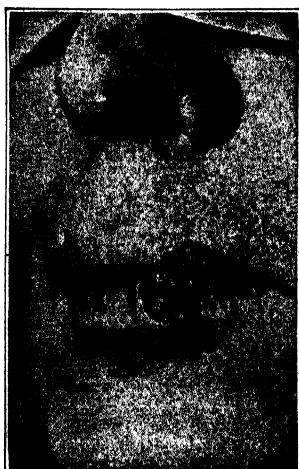


Fig. 98.—Chancre of lip. (From Sutton and Sutton: *Diseases of the Skin*. The C. V. Mosby Co.)

4. In a short time symptoms of systemic involvement appear.
5. The systemic manifestations disappear to be followed at once or after years by involvements of the internal organs.

This typical evolution which does not occur in every case, even a chancre being absent or undetected in some cases, gives rise to the following *stages* of syphilis which are useful for descriptive purposes:

1. *Stage of Incubation.*—From the time of infection to the appearance of the chancre, usually from two to six weeks; most often three or four weeks.

2. *Primary Stage*.—Beginning with the appearance of the chancre and ending with the development of a skin eruption or other manifestations of systemic involvement. This stage usually lasts from about eight to twelve weeks. After the chancre has persisted for from four to six weeks it heals. This is followed by a period of from four to eight weeks before the appearance of the secondary manifestations, during which the patient shows no objective signs but may suffer malaise, anemia, etc. This is often called the *primary latent period*.
3. *The Secondary Stage or Stage of Systemic Involvement*. This stage is characterized by such symptoms as loss of hair, skin eruptions, general adenopathy, and the appearance of mucous patches in the mouth and throat. The duration is from a few weeks to several months.
4. *The Latent Stage*.—This is a period that follows the secondary stage, during which the patient shows no signs of the disease and the disease is recognized only by means of serological tests. This stage may last for only a few months or for a lifetime. Its average length is six or seven years.
5. *Tertiary Stage*.—This stage follows the latent stage and is characterized by the destruction of tissues and the development of gummas.

Prenatal (Congenital) Syphilis.—The only manner in which a child in utero can contract syphilis is from the mother. The organisms are transmitted through the placenta. A syphilitic father can transmit the infection to his child only indirectly; i.e., by infecting the mother. The shorter the time elapsing between infection of the mother and conception, the more likely is the fetus in utero to become infected. If adequate treatment of the mother is instituted before the fifth month of pregnancy, the child is almost sure to be born free of syphilis. The manifestations of prenatal syphilis are further discussed in the section on Pathology (page 522).

Immunity.—Although antibody formation comparable to that in such diseases as typhoid fever, etc., does not occur in syphilis, a person develops some kind of resistance to the

disease, because when he has syphilis he is not susceptible to a second syphilitic infection. When he is completely cured, however, susceptibility becomes as great as ever. The blood serum of a patient with syphilis contains a substance, not found in normal blood, which is capable of combining with extracts of normal muscle tissue, especially the heart muscle of the ox, and destroying complement or causing precipitation. Upon this phenomenon are based the complement fixation or Wassermann test, and such precipitation tests as the Kahn and Kline tests for syphilis. There is no method of artificially producing an active or passive immunity against syphilis. Insufficient early treatment may be of greater harm than good because it fails to effect a cure and at the same time retards the establishment of an immunity.

Laboratory Diagnosis.—The laboratory has at its disposal three important procedures applicable to the diagnosis of syphilis; namely, (1) the demonstration of the organisms in the lesions by means of the dark-field microscope, (2) the complement fixation (Wassermann) test, and (3) precipitation tests. The second and third are performed on the blood serum. The use of the dark-field microscope to demonstrate *Treponema pallidum* has its most practical application in the investigation of suspected chancres. During the first few days of a chancre the organisms may be found in almost all cases. As the age of the chancre increases, the less likely is *Treponema pallidum* to be found and the more likely is the complement fixation test to be positive. The complement fixation test is seldom positive during the first few days of the chancre but usually becomes positive before the appearance of secondary manifestations. It is positive in about 98 per cent of cases of syphilis during the secondary stage. Positive results are somewhat lower (80 to 90 per cent) in tertiary syphilis. In paresis both blood and cerebrospinal fluid show positive results in about 100 per cent of cases. In tabes dorsalis and syphilitic meningo-arteritis the complement fixation test on the cerebrospinal fluid is positive in more than 90 per cent of cases and on the blood serum in about 80 per cent of cases. The results of the precipitation tests, except

in the cerebrospinal fluid, closely parallel those of the complement fixation test. The colloidal gold test is of value in determining the type of syphilitic involvement of the central nervous system.

The complement fixation test, regardless of the technic used, is usually referred to as the Wassermann test because August von Wassermann first applied the principle of complement fixation to the diagnosis of syphilis. The test has been so much improved that about all that remains of the original test is the principle and the name.

Prevention.—The patient is most likely to convey syphilis during the primary and secondary stages because chancres and mucous patches are practically living cultures of syphilis organisms. Those attending patients with these lesions should be careful not to come in contact with the patient's secretions. Patients should not be allowed to use articles used by others. Since syphilis is so prone to apparent cures followed by relapses, great caution should be exercised in pronouncing a patient cured. All manual examinations should be made with gloves, because a patient may show no evidence of syphilis but at the same time be capable of transmitting the infection. People should be educated as to the universal prevalence of syphilis, the uncertainty of its cure, and the danger of syphilis not only to the person who has it but also to his marriage partner and his children.

Relation Between Syphilis and Yaws.—Yaws or frambesia is a tropical disease that has a close clinical resemblance to syphilis and is caused by an organism (*T. pertenue*) that bears a close resemblance to *T. pallidum*. It is believed by some that yaws was but a special form of syphilis, but most observers believe that they are distinct diseases.

II. Relapsing Fever

Relapsing fever is an acute infectious disease that is caused by several varieties of spirochetes and is characterized clinically by alternating periods of febrile illness and apparent recovery. The spirochetes are found in the peripheral blood during the febrile attacks and are transferred from man to

man by certain species of lice, ticks, bedbugs, and possibly other biting insects. Recent investigation indicates that a reservoir of infection exists in some small animal.

III. Rat-Bite Fever

Rat-bite fever is a specific infectious disease due to *Spirillum minus* that occurs primarily in wild rats. It is spread from rat to rat and from rat to man by the bite of the rat. It is characterized by ulceration at the site of infection, fever, and a skin eruption. The organisms may be found in the ulcer by smears or dark-field illumination. Rat-bite fever is not a common disease but is world-wide in its distribution. Little is known about immunity in this disease.

IV. Infectious Jaundice

Infectious jaundice (Weil's disease) is an epidemic disease characterized by jaundice, fever, and splenic enlargement. It is caused by a spirochete which is found infecting rats throughout the world. Man probably acquires the infection through the skin from soil contaminated with the urine of infected rats or through the mouth by food or water that has been contaminated in the same manner. The spirochetes may be found in the blood in the very early days of the disease and in the urine after the seventh day. An attack of the infectious jaundice is followed by a lasting immunity.

V. Fusospirillary Infections

This is a condition of the throat or mouth that is characterized by the formation of a pseudomembrane beneath which ulceration occurs. When primarily attacking the tonsils and pharynx, it is known as Vincent's angina; when occurring primarily on the gums and in the mouth, it is known as trench mouth. The disease is important both within itself and because the membrane may be mistaken for a diphtheritic membrane, while the extensive ulceration may cause the disease to be confused with syphilis.

Associated with the lesions are two organisms. One is a fusiform bacillus and the other is a spirochete or spirillum.

This is the reason for such infections being spoken of as fusospirillary infections. In early cases the bacilli are most numerous, while in the late cases the spirilla are most numerous. Other organisms are often present. It has never been proved conclusively that these organisms are the sole cause of this condition, and some workers believe that they are only secondary invaders. Whether cause of secondary invader, it does seem that their relation to this condition is an

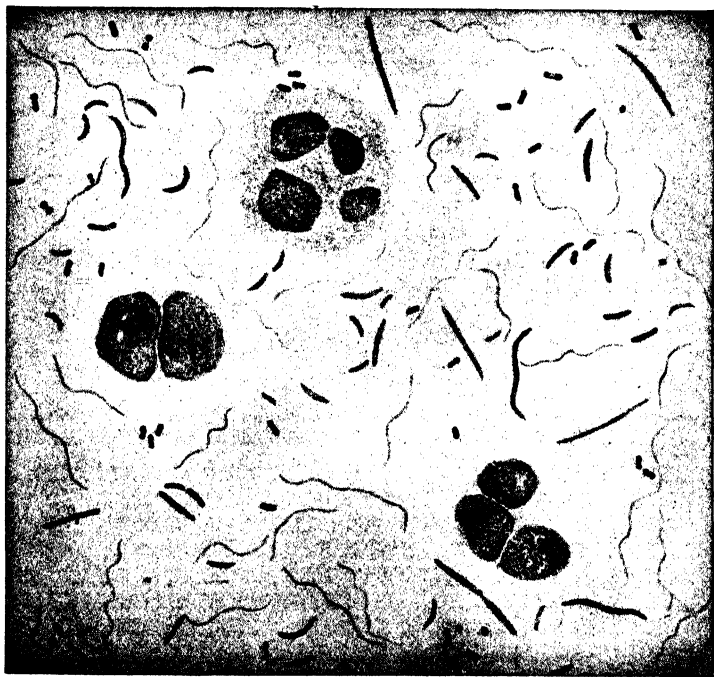


Fig. 99.—Organisms of Vincent's angina. Note that the spirilla and fusiform bacilli are distinct in appearance. (From Ford: *Textbook of Bacteriology*. W. B. Saunders Co.)

important one. Whether the bacillus and spirillum are separate organisms growing in symbiosis or one represents a stage of the development of the other is an unsettled question. Most investigators hold the latter view. The organisms are susceptible to the action of penicillin.

The disease is spread by the discharges from the mouth and throat which should be cared for in the same manner

as those from a case of diphtheria. The bacteriological procedure to be followed when a pseudomembranous inflammation of the throat is encountered was discussed on page 290.

VI. Other Spirochetes and Related Organisms

1. *Spirochaeta buccalis*, *Spirochaeta dentium*, and *Treponema macrodentium* are nonpathogenic organisms found in the mouth. They may cause confusion when examining material from the mouth for syphilis.

2. *Borrelia refringens* is found in the mouth and in association with *Treponema pallidum* in various syphilitic lesions.

Questions for Review

1. Discuss the different stages of syphilis.
2. List three important procedures applicable in the diagnosis of syphilis.
3. How is trench mouth spread?
4. What is the relation between Vincent's angina and trench mouth? What is their cause?

True-False Test

Place the word "true" or "false" before each statement.

- 1. The organism causing syphilis is very easily stained.
- 2. The organism causing syphilis, when introduced into the body, multiplies rapidly and spreads over the body by the lymph and blood streams.
- 3. It is thought that syphilis was carried to Europe by sailors returning with Columbus from the New World.
- 4. Syphilis is acquired by indirect contact only.
- 5. If adequate treatment of the mother is instituted before the fifth month of pregnancy, the child is almost sure to be born free of syphilis.
- 6. There is a permanent immunity developed following an attack of syphilis.
- 7. Yaws is a special form of syphilis.
- 8. Rat-bite fever is a common specific infectious disease.

Completion Test

1. Diseases caused by spirochetes are -----, -----, and -----.
2. Syphilis acquired through the placenta is known as ----- syphilis.
3. The organism causing syphilis is known as the -----.

4. The two most important diagnostic features of the above organism are ----- and -----.
5. The patient is most likely to convey syphilis during the ----- and ----- stages.
6. Relapsing fever is transferred from man to man by -----, -----, and -----.

References

- Zinsser and Bayne-Jones: Textbook of Bacteriology, New York, 1939, D. Appleton-Century Co.
- Rosenau, Milton J.: Preventive Medicine and Hygiene, New York, 1935, D. Appleton-Century Co.
- Mead, Sterling V.: Diseases of the Mouth, St. Louis, 1940, The C. V. Mosby Co.
- Howles, J. K.: Synopsis of Clinical Syphilis, St. Louis, 1943, The C. V. Mosby Co.
- Various authors: Vincent's Infection—A Wartime Disease, Am. J. Pub. Health 35: 433-451 (May), 1945.

CHAPTER XXXIII

FUNGI

I. General Characteristics

Molds, yeasts, and the moldlike forms of the higher bacteria constitute the group of organisms known as *fungi*. Fungi do not contain chlorophyl and are probably degenerate forms of chlorophyl-bearing ancestors, most likely the algae. Some fungi, for example mushrooms and toadstools, are of considerable size, but the ones of medical importance are microscopic in size or at least so small that the microscope is necessary for their complete investigation. The fungi are of importance in the processes of nature, agriculture, manufacturing, and medicine. The science that treats of fungi is known as *mycology*. A fungus infection is known as a *mycosis*.

A. MOLDS

Molds are made up of a network of branched threads bearing fruiting bodies. The network is known as a *mycelium* and the individual threads are known as *hyphae*. In some molds the hyphae consist of single threads containing many nuclei. In others the thread is divided by cross walls or septae into distinct cells, each containing a nucleus. The hyphae have thin walls which allow them to absorb food and water readily. This accounts for their rapid growth. The fruiting body is the portion that appears most prominent when the mold is observed. The essential part of the fruiting body is the spore which is the reproductive portion of the mold. The spores of molds should not be confused with bacterial spores which are resistant bodies formed by bacteria, not for the purpose of multiplication, but for the purpose of preserving themselves when subjected to adverse influences. In some molds the spores are simply attached to the hyphae; in some the hyphae are branched to form brushlike processes each of which bears a spore; in others the hyphae produce heads from which radiate fine chains of spores, and

in still others the hyphae bear little pods or sacs in which the spores rest. Many of the spore-bearing hyphae project into the air (aerial hyphae).

Conditions Affecting Growth of Molds.—Molds grow best under much the same conditions as bacteria; i.e., in warm moist surroundings and in the absence of direct sunlight. They are capable of growing in the presence of much more acid than are the bacteria and are capable of growing in the presence of large amounts of sugar, which is not the case with bacteria. They do not grow in the absence of free oxygen and are killed by comparatively low temperatures. Although moisture aids in the growth of molds, many species require less moisture than bacteria.

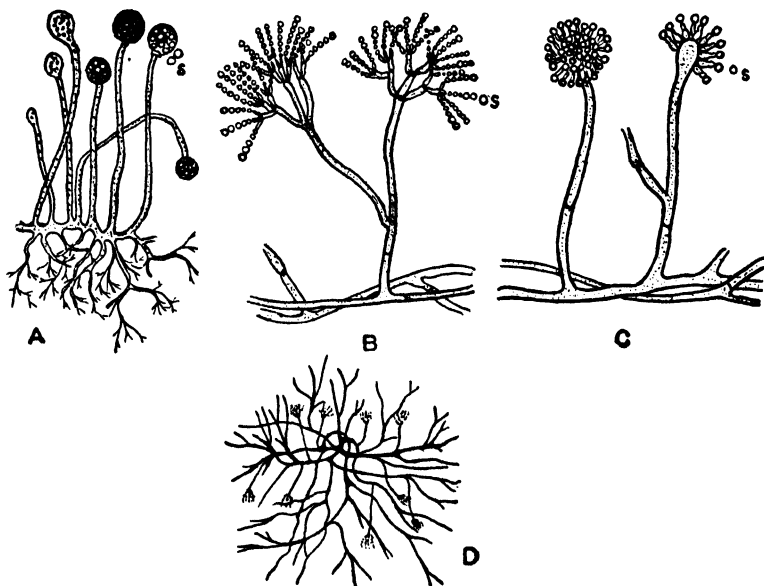


Fig. 100.—Some common molds. Note the fruiting bodies in which the reproductive spores (*S*) are formed. *D* represents the mycelium of which a mold is composed. (From Burdon: *A Textbook of Bacteriology*. By permission of The Macmillan Co., publishers.)

Reproduction of Molds.—Molds reproduce by the sexual or asexual conversion of a spore into a vegetative mold. In most cases the spores become separated from the hyphae before reproducing. Spores are resistant to drying, cold,

and moderate heat, and may maintain their vitality for a long time. They are constantly present in the air, and when they come in contact with food or other material that supplies the necessary elements for growth, they develop into new molds. In asexual reproduction the spores simply become converted into hyphae. If the spores are enclosed in a sac, the sac ruptures before this happens. In sexual reproduction the spores of two hyphae fuse, separate from the hyphae, and become surrounded by a thick capsule in which a new mold is produced.

Classification of Molds.—There are many classifications of molds, but one that is probably as satisfactory as any is into (1) the *common molds* that contaminate foods and culture media but seldom cause disease, and (2) the *Hyphomycetes* or disease-producing molds.

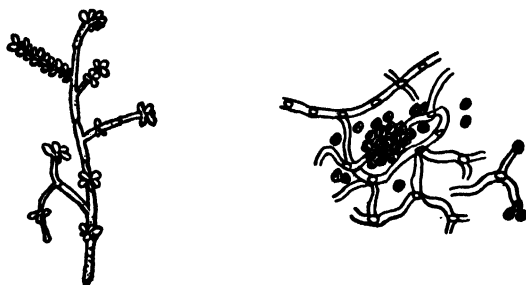


Fig. 101.—Pathogenic molds. The mold on the left is the cause of sporotrichosis. The one on the right is the cause of pityriasis versicolor, a parasitic skin disease. (From Burdon: *A Textbook of Bacteriology*. By permission of The Macmillan Co., publishers.)

Importance of the Common Molds.—Common molds are capable of injuring woodwork and fabrics and may render food unfit for use. They may injure or destroy food during its growth, in the process of manufacture, or after it has reached the home. Foods most often attacked are bread, vegetables, fruits and preserves. Molds are an important factor in the decay of dead animal and vegetable matter in which complex organic compounds are broken down into simple ones and returned to the soil to be used as food by the green plants. Some (ex. certain mushrooms) are sources of food for man. Molds are used commercially in the manufac-

ture of beverages and to give flavor to certain kinds of cheese (Roquefort, Camembert, etc.). Penicillin, a most effective antibacterial substance, is derived from a common mold, *Penicillium notatum*. Certain molds, especially *Aspergilli*, have been found in infected wounds and in infections of the nose, eyes, and skin. *Aspergillus* infection of the lungs (pulmonary aspergillosis) bears a close clinical resemblance to tuberculosis.

B. YEASTS

General Characteristics.—Yeasts are lower forms of life than the molds but are more highly developed than the bacteria. In common with the molds and bacteria, yeasts are dependent plants, i.e., they contain no chlorophyl. They are unicellular organisms, nonmotile and usually round or oval in shape. They show considerable variation in size, depending on age and species, but all are microscopic. Nuclei may be demonstrated by suitable stains. The cytoplasm is divided into endoplasm and ectoplasm and contains various granules and vacuoles. They have thin cell walls of cellulose. There are more than forty species of yeasts, some of which are of importance while others are not.

Reproduction of Yeasts.—Most yeasts multiply by the process of budding; one genus divides by simple fission, and under certain conditions all multiply by spore formation. In the process of budding the nucleus moves toward the edge of the cell and divides into two daughter nuclei. A knoblike protrusion of the cytoplasm forms at this point and one of the nuclei passes into it. The protrusion increases in size and becomes constricted at its base until there is only a narrow connection between the protrusion and the parent cell. Finally the two separate and the protrusion or bud which is now a small yeast cell continues to grow until it reaches full size and the process is repeated. Multiplication by fission, which is characteristic of one genus, resembles the vegetative multiplication of bacteria. The yeast develops to its full size and a membrane forms across the middle. A dividing wall forms and the two parts separate. In reproduction by spore formation the cell enlarges slightly

and the nucleus becomes converted into a definite number of spores. In some yeasts only one spore is formed, but in most of them four or eight are formed. The spores absorb water and break through the wall of the parent cell to form new yeast cells. Spore formation does not occur when the yeasts are developing under the most suitable conditions.

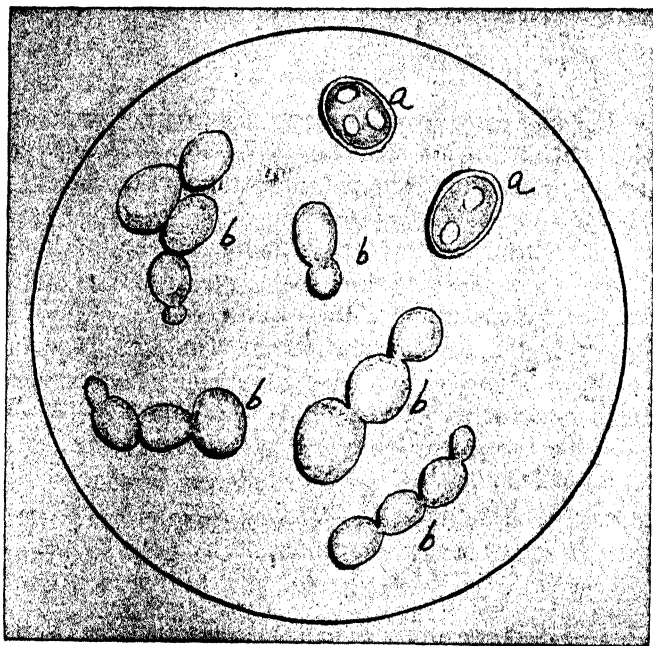


Fig. 102.—Yeast cells. *a*, Adult cells; *b*, budding cells.

Classification of Yeasts.—From a pathological standpoint yeasts may be classified as *Saccharomyces* (sugar fungi) and *Blastomyces* (pathogenic yeasts). From a commercial standpoint the former may be classified as wild yeasts which are constantly present in the air and cultivated yeasts which were originally wild yeasts but are now being grown artificially and used commercially.

Fermentation.—Yeasts play an important part in the process of fermentation; in fact, this is their most important activity. Fermentation was discussed on page 87.

Conditions Affecting Growth of Yeasts.—Yeasts grow best in the presence of moisture. They require organic food material and a temperature of from 23° to 40° C. Pathogenic yeasts grow best at body temperature (37.5° C.). They will grow in the presence of more acid than will bacteria. In fact they grow best on food material that is slightly acid. Their vitality is remarkable, some having been known to remain alive for twelve years.

Economic Importance of Yeasts.—The chief economic importance of yeasts depends on their fermentation of sugars, converting them into alcohol and carbon dioxide, which is practically applied in the manufacture of alcoholic beverages and in baking. In the manufacture of alcoholic beverages carbon dioxide is a by-product, while in baking it is the essential factor. When the yeasts are mixed with dough, they multiply and their enzymes ferment the sugars present, producing alcohol and carbon dioxide. The carbon dioxide, which is a gas, escapes and fills the dough with small holes which cause it to "rise." When the bread is baked the carbon dioxide expands further and the alcohol is volatilized. This gives the bread a texture that renders it palatable and easily digested.

Commercial yeast is prepared by growing the yeasts in suitable liquid culture media, separating them from the liquid portion of the medium by centrifuging, and then mixing them with starch or vegetable oil, moulding, and cutting into cakes. Many therapeutic claims have been made for yeast but many of them remain unproved. Yeast, however, is a source of vitamin B and of ergosterol from which vitamin D is obtained.

II. Diseases Caused by Fungi

A. THE DERMATOMYCOSES

Superficial fungus infections of the skin, such as ringworm and favus, which have no tendency to invade the deeper structures of the body are known as *dermatomycoses*. Fungi causing dermatomycoses are often spoken of as *dermatophytes*. Of the dermatophytes there are four impor-

tant genera: namely, (1) *Microsporon*, (2) *Trichophyton*, (3) *Epidermophyton*, and (4) *Achorion*. The dermatophytes are closely related from the standpoint of disease production but bear little botanical relation to each other.

Microspora are the most common cause of ringworm of the scalp and may give rise to ringworm in other parts of the body. Hairs removed from the affected regions are surrounded by a coat of spores, and a few mycelia may be

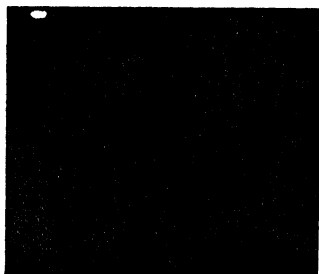


Fig. 103.

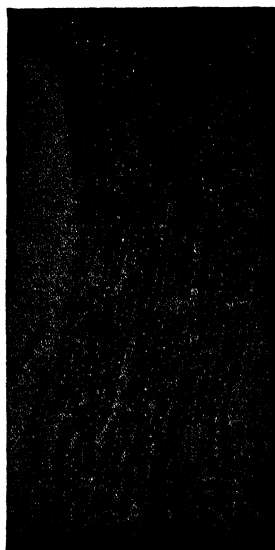


Fig. 104.

Fig. 103.—Hair infected with microspora. (From Bruhns-Alexander: Grundriss der Mykologischen Diagnostik. Julius Springer, Berlin.)

Fig. 104.—Trichophyton in hair. (From Bruhns-Alexander: Grundriss der Mykologischen Diagnostik. Julius Springer, Berlin.)

found. Scales of skin from the affected area may show many branched mycelia. *Trichophyta* may cause ringworm of the scalp, beard, skin, or nails. The organisms are found as chains of spores inside or on the surface of hairs taken from affected areas. *Epidermophyta* are largely responsible for ringworm of the body, hands, feet, and nails. *Epidermophyta* grow only in the epidermis when they appear as interlacing threads. They do not invade the hairs. *Achorion schoenleinii* is the most characteristic form of *Achorion* and

is the cause of almost all cases of favus. The spores and mycelia are found in the favus crusts. Hairs in the affected areas are filled with vesicles and channels from which the mycelia have disappeared.

Ringworm of the scalp occurs most often in children and is a common and highly communicable disease. It may be spread directly from person to person or by articles of apparel. It occurs in domestic animals from which it may be transmitted to man. Ringworm of the beard is known as barber's itch. Epidermophytosis is ringworm of the axilla, groins, hands, feet, or nails. Ringworm of the groins is known as *tinea cruris* or dhobie itch. Ringworm of the feet is known as athlete's foot. Epidermophytosis may be contracted by direct or indirect contact. Athlete's foot is contracted from footwear, lockers, floors, etc., and is difficult to control. Favus usually affects the scalp and is characterized by the formation of crusts about the mouth of the hair follicles. These crusts consist of masses of spores and mycelia mixed with leucocytes, epithelial cells, etc. It may be transmitted directly or indirectly from person to person, or it may be contracted from domestic animals, such as cats and dogs.

The laboratory diagnosis of the dermatomycoses depends on demonstrating the fungi in the hair and skin scrapings by direct microscopic examination or by cultural methods. Fungi are rendered more visible by soaking the material to be examined in from 10 to 20 per cent sodium or potassium hydroxide before examining.

The control of the dermatomycoses is a very difficult matter. It consists in the proper sterilization of clothing, bathing suits, and objects subject to frequent handling. Hygiene of the feet and swimming pools is of extreme importance.

B. ACTINOMYCOSIS

Actinomyces is an infectious disease of lower animals (especially cattle) and man that is caused by several species of fungi belonging to the genus *Actinomyces*. Of these *Actinomyces bovis* is most important. Actinomycosis is characterized clinically by the formation of nodular swellings

which soften and form abscesses that discharge a thin pus through multiple sinuses. Almost any part of the body, such as the lungs, intestines, and bones, may be involved, but the most common site of infection is the skin and subcutaneous tissue, especially about the lower jaw. The disease in cattle is known as lumpy jaw.

The causative fungus is found in the pus or in the walls of the abscesses as small yellow granules about the size of a pinhead. They are known as *sulphur granules*. When a sulphur granule is placed on a slide and a cover glass is pressed down upon it, a characteristic microscopic picture is seen; namely, a central threadlike mass from which radiate many clublike structures. For this reason actinomyces are often spoken of as *ray fungi*. The clubbed appearance is not very pronounced in cultures.

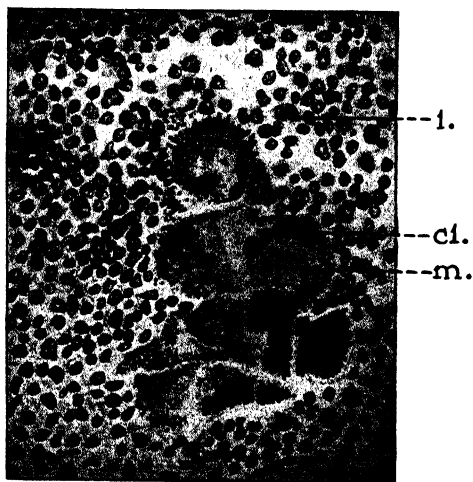


Fig. 105.—Actinomyces. *cl.* Clubs; *m.* mycelium; *l.* leucocytes. (From Bell: *A Textbook of Pathology*. Lea and Febiger.)

It was originally thought that cattle became infected by eating grain contaminated with the causative organism and that man became infected by holding a piece of contaminated straw in his mouth as is often the habit of farmers and stockmen. Recent investigators have questioned this view, holding that the actinomyces found on grain are non-

pathogenic, and they further state that in some people pathogenic actinomyces are normal inhabitants of the mouth. The organisms invade the deeper tissues through bad teeth or wounds in the mouth. Recent studies have shown that organisms other than actinomyces may produce lesions clinically and pathologically indistinguishable from actinomycosis.

The laboratory diagnosis of actinomycosis is made by finding objects in the discharges that are both grossly and microscopically sulphur granules or by demonstrating them in sections of tissue taken from the lesions. Cultural methods are of value.

C. SPOROTRICHOSIS

Sporotrichosis is a chronic infection usually limited to the skin and underlying tissues and is characterized by the formation of gumma-like growths that slowly undergo softening and ulceration. In typical cases the lesions form a chain extending along the arm. The disease is peculiar in that it may affect man, the lower animals, or plants.

Sporotrichosis is caused by several species of fungi belonging to the genus *Sporotrichum*. Sporotricha are widely distributed in nature, and infection in man may take place in various ways. Probably the most common mode of infection is the introduction of the organisms into wounds by infected plants or vegetable matter. Transmission of the infection from lower animals to man by bites or indirect routes has been recorded. When found in smears from the pus or in sections of tissue taken from the lesions sporotricha appear as oval or cigar-shaped structures and are often found within the mononuclear cells. As a rule, however, their demonstration is accomplished only by cultural methods.

D. BLASTOMYCOSIS

Blastomycosis is a granulomatous and suppurative inflammation that is characterized by the formation of multiple abscesses in the skin and subcutaneous tissues (blastomycetic dermatitis) or in the internal organs of the body (systemic blastomycosis). The cutaneous form of blastomycosis

is more common than the systemic form. Of the systemic forms pulmonary blastomycosis is most common.

Blastomycosis is caused by one or more species of yeast-like organisms belonging to the genus *Blastomyces*. They may be demonstrated by cultural methods or direct microscopic examination of pus from the lesions. In pus from the lesions *Blastomyces* occur as round or oval granular highly refractile bodies varying from 5 to 20 microns in diameter. They are surrounded by a distinct capsule and budding forms are often present. They grow rather characteristically on all media, but their isolation is often rendered difficult by the overgrowth of bacterial contaminants of the lesion. *Blastomyces* may be found on all kinds of vegetable matter but the source and mode of human infection is still an unsolved problem. Accumulated evidence, however, indicates that cutaneous blastomycosis is due to infections through wounds, and the finding of a primary focus in the lungs in systemic blastomycosis indicates that systemic infections are often acquired by way of the respiratory tract. It also seems certain that in some cases of systemic blastomycosis infection occurs by way of the skin.

E. COCCIDIOIDAL GRANULOMA

Coccidioidal granuloma is a disease which bears considerable resemblance to blastomycosis and is caused by *Coccidioides immitis*, a yeastlike fungus that closely resembles the blastomyces. The disease is ordinarily more acute and severe than blastomycosis. The majority of cases have been found in California. The exact mode of infection has not been determined. One view is that some insect, feeding on either contaminated soil, vegetation, or infected rodents, transmits the infection to animals and man. The organism is widely distributed in nature.

F. TORULA INFECTIONS

The torulae are a group of yeastlike organisms that most often cause infections of the lungs or central nervous system but may attack other parts of the body. The disease is char-

acterized by the formation of multiple small nodules that have the gross and microscopic appearance of tubercles. In involvements of the central nervous system the meninges are thickened and matted together. Infection with torulae is known as torulosis. Torulosis can be diagnosed with certainty only by finding torulae in the affected tissues, pus, sputum, cerebrospinal fluid, etc.

G. MONILIA INFECTIONS

Moniliae are yeastlike organisms of which there are many species that produce a variety of lesions in man and which are usually limited to the skin or mucous membrane but may involve the internal organs. Infection with moniliae is known as moniliasis. The most important types of moniliasis are thrush and bronchopulmonary moniliasis.

Thrush.—Thrush, which is caused by *Monilia albicans*, is characterized by the occurrence on the inside of the lips, on the hard palate, and on the tips and edges of the tongue of small milklike flecks which may coalesce and cover the mucous membrane of the entire mouth. Beneath the patches are areas of catarrhal inflammation. The causative agent is spread from person to person by contaminated fingers, utensils, and nipples. Thrush is rare in healthy subjects of any age but is comparatively common in ill-nourished children. It may occur as a vaginal infection in ill-nourished women, especially during pregnancy.

Bronchial and Pulmonary Moniliasis.—Infections due to moniliae are of at least some importance as causes of pulmonary disease. The symptoms vary from those of a mild inflammation to those of a severe infection like tuberculosis. A diagnosis is established by demonstrating the causative organism in the sputum.

Sprue (Psilosis).—Sprue is a chronic wasting disease that is characterized by a marked loss of weight, a profound anemia, and periods of diarrhea and excessive intestinal fermentation alternating with periods of improvement. It occurs chiefly in Europeans inhabiting the tropics. It has been suggested that some of the cases diagnosed as pellagra

in the Southern States are in truth sprue. *Monilia psilosis* was once thought to be the cause of disease. The prevailing opinion indicates that the underlying factor is a fault of metabolism which produces a condition of the intestinal tract that allows *Monilia psilosis* to implant itself and multiply, whereas under normal conditions these moniliae pass through the intestinal canal without becoming implanted. Cases developing in persons without apparent dietary imbalance suggest that, at least in some cases, infection alone may cause sprue. Sprue is a serious disease and unless properly treated ends fatally.

H. ERGOTISM

Ergot, a drug widely used to check hemorrhage, especially after childbirth, is composed of several alkaloidal poisons produced by the growth of a mold *Claviceps purpurea* in the grains of wheat, rye, and barley. When bread made from infected grain is eaten, the condition known as *ergotism* develops. Ergotism is characterized by such manifestations as contraction of smooth muscle, gangrene of the extremities, and abortion. It was at one time one of the most common diseases of Central Europe.

I. MOLDS AND PLANT DISEASES

Molds are of great economic importance because they cause so many diseases of plants. So important are they as causes of plant diseases, that plants and vegetables imported from other countries are rigidly inspected upon arrival in our ports and if found infected are denied admittance. Among important plant diseases due to molds may be mentioned:

1. Brown rot of peaches and plums.
2. Chestnut blight.
3. Mildew of grapes.
4. White pine blister rust.
5. Rust of oats, wheat, barley, etc.
6. Smuts of various grains.
7. Potato rot.

Questions for Review

1. Give the equation for the breaking down of grape sugar into alcohol and carbon dioxide.
2. How may fungus infections of the skin be controlled?
3. What is blastomycosis?
4. How is thrush spread from person to person?
5. What is the cause of sprue?

True-False Test

Place the word "true" or "false" before each statement.

- 1. Molds grow best under much the same conditions as bacteria.
- 2. Yeasts contain no chlorophyll.
- 3. Yeasts play a small part in fermentation.

Completion Test

1. ----- and ----- belong to the group of organisms known as fungi.
2. A fungus infection is known as a -----.
3. The science that treats of fungi is known as -----.
4. The most effective antibacterial substance derived from a common mold is -----.
5. When yeasts are mixed with dough -----, -----, and ----- are produced.
6. Superficial fungus infections of the skin are known as -----.
7. Ringworm may be spread directly from person to person by -----.
8. Ringworm of the beard is known as -----.
9. Ringworm of the feet is known as -----.
10. Actinomycosis in cattle is known as -----.

References

- Dodge, Carroll W.: Medical Mycology, St. Louis, 1935, The C. V. Mosby Co.
- Swartz, Jacob Hyams: Elements of Medical Mycology, New York, 1943, Grune & Stratton, Inc.
- Conant, Martin, Smith, Baker, and Callaway: Manual of Clinical Mycology, Philadelphia, 1945, W. B. Saunders Co.
- Lewis and Hopper: An Introduction to Medical Mycology, Chicago, 1943, The Year Book Publishers, Inc.

CHAPTER XXXIV

THE PROTOZOA

I. General Characteristics

The animal kingdom is divided into two great divisions, the *Metazoa* which are multicellular organisms, and the *Protozoa* which are morphologically unicellular organisms and are the lowest form of animal life. Protozoa occupy about the same relative position in the animal kingdom that the bacteria occupy in the plant kingdom. They are more complex in structure and functional activity than the average cell of a multicellular organism and have structural differentiations for the performances of such special functions as procuring food, locomotion, respiration, excretion, and attachment to other objects. These structures are known as organelles. It is thus apparent that protozoa are more complex in structure and life cycle than bacteria; i.e., they are higher forms of life. The vast majority are of microscopic size and, as a rule, the pathogenic ones are smaller than the nonpathogenic ones. They may be spherical, spindle, spiral or cup-shaped.

Structure of Protozoa.—Protozoa are composed of protoplasm differentiated into cytoplasm and a nucleus or nuclear material. Some have more than one nucleus. The cytoplasm is often separated into a hyaline or homogeneous ectoplasm and a granular endoplasm. The ectoplasm helps form the various organs of locomotion, contraction, and prehension, such as pseudopods, flagella, cilia, and suckorial tubes. The endoplasm digests food materials and surrounds the nucleus. In certain species of protozoa the ectoplasm contains a definite opening for the ingestion of food. Some are surrounded by a membranous or shell-like structure. Such enclosing structures are not found in any of the pathogenic protozoa except when they are in the cyst form.

Nutrition.—Many protozoa, especially the pathogenic ones, absorb fluid directly through the body wall. The majority are capable of taking in solid food, such as small animal or

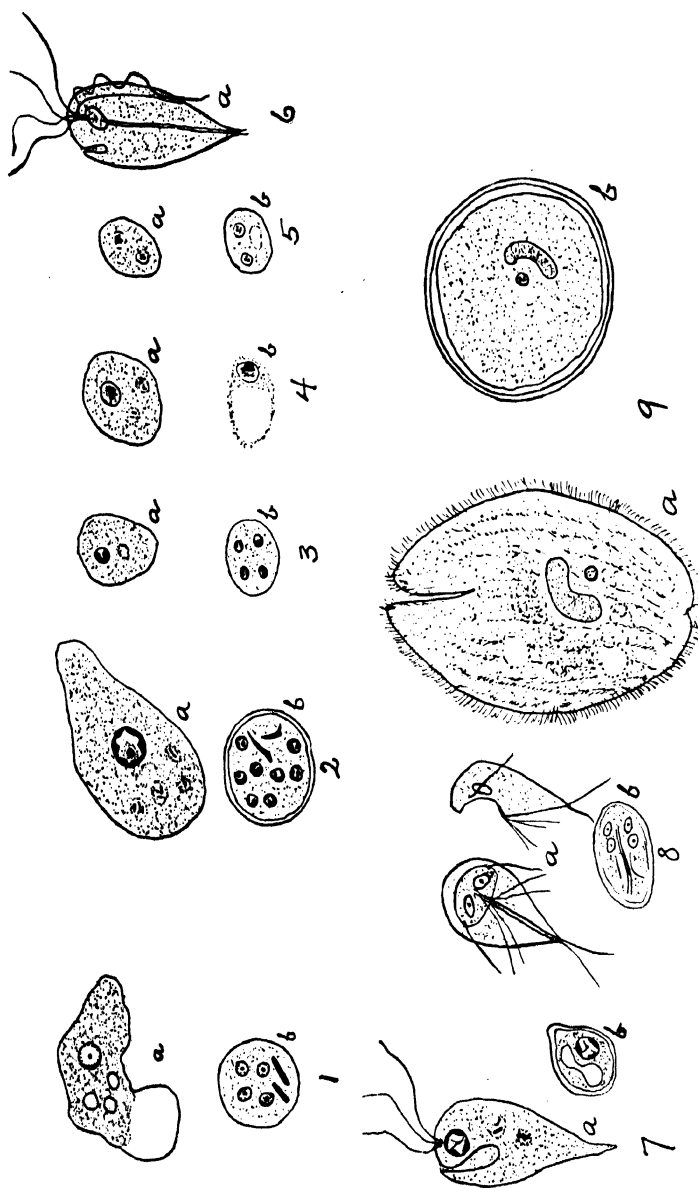


Fig. 106.—Diagram illustrating protozoa (a, vegetative forms; b, cysts). 1, *Endameba histolytica*; 2, *Endameba coli*; 3, *Endolimax nana*; 4, *Iodameba williamsi* (Duetschli); 5, *Dielameba fragilis*; 6, *Trichomonas hominis* (intestinalis); 7, *Chilomastix mesnii*; 8, *Giardia lamblia*; 9, *Balantidium coli*. (From Bray: *Synopsis of Clinical Laboratory Methods*. The C. V. Mosby Co.)

vegetable organisms, and digesting them in their own bodies by enzymes secreted by their cytoplasm. Some have a special portal for ingesting food. Their food seems to consist chiefly of bacteria, and for this reason may be of importance in limiting the bacterial population of the Universe. Their waste material is excreted through the cell wall or, in the case of some, through an ejection pore.

Motility.—All protozoa possess some type of motility. It may be accomplished by pseudopod formation or by the action of flagella or cilia. In locomotion by *pseudopod* (false foot) formation a sharp or blunt protoplasmic process derived from the ectoplasm flows forward, and the remainder of the organism follows it. *Flagella* are whiplike prolongations of the protoplasm which by their lashing movements produce motility. Of the protozoa that have flagella some have only one, others have several. Some of the flagellate

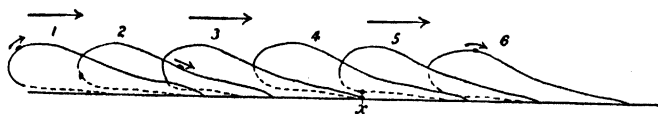


Fig. 107.—Diagram illustrating ameboid motion. Note how the particle of soot attached to the surface of the amoeba moves as the amoeba progresses. (From Jennings.) (From Shull: *Principles of Animal Biology*. McGraw-Hill Book Co.)

protozoa also have an *undulating membrane* which plays an important part in locomotion. This is a fluted membranous protoplasmic process attached to one side of the organism. *Cilia* are similar to flagella except that they are shorter, more delicate, and more plentiful. Individually they are less powerful than flagella but the synchronous action of the many cilia that are present accomplishes the most rapid motion of which unicellular organisms are capable. Some protozoa move by means of both flagella and pseudopods.

Cyst Formation.—When protozoa are subjected to adverse conditions they become inactive, assume a more or less rounded form, and surround themselves with a resistant membrane within which they may live for a long time and withstand various destructive agents. This is known as *cyst* formation. When conditions suitable for the growth

of the organism are re-established, the cyst imbibes water and the organism returns to the vegetative state. In some cases cyst formation precedes reproduction. Since vegetative protozoa are very susceptible to deleterious influences and cysts are very resistant, it is the latter that are usually responsible for the spread of protozoan infections.

Reproduction.—Protozoa may undergo either sexual or asexual reproduction. In some species a sexual cycle occurs in one species of animal and an asexual cycle occurs in another. The host in which the sexual cycle occurs is known as a *definitive* host; the one in which the asexual cycle occurs is known as an *intermediate* host. Protozoan cells capable of sexual reproduction are known as *gametes*. The cell formed by the union of two gametes is known as a *zygote*.

Classification.—Based chiefly on their method of locomotion, protozoa are divided into four classes, namely:

1. Sarcodina—characterized by locomotion by pseudopods and division of the cytoplasm into ectoplasm and endoplasm. Represented by the pathogenic and nonpathogenic amebas.

2. Mastigophora or Flagellates—protozoa that are characterized by locomotion by means of flagella and an undulating membrane. They have two nuclei and the cytoplasm is not differentiated into endoplasm and ectoplasm. Their bodies are often pear-shaped and fixed in outline. The most important flagellates from the medical standpoint are the Trypanosoma, Leishmania, and intestinal flagellates.

3. Sporozoa—characterized by absence of external organs of locomotion. They live in the cells, tissues, and cavities of the body and are represented by the Plasmodium of malaria.

4. Ciliata—characterized by a distinct and constant form and by the presence of cilia for locomotion. The only pathogenic member of this group is *Balantidium coli*.

II. Diseases Caused by Protozoa

A. MALARIA

Malaria is an acute febrile disease caused by the malaria parasite which undergoes an asexual cycle of development

in the red blood cells of man and a sexual cycle within the *Anopheles* mosquito. The parasite is a protozoon belonging to class Sporozoa and genus *Plasmodium*.

Types of Malaria.—Malaria occurs in three* rather characteristic types, each of which is caused by its own distinct species of *Plasmodium*. These types are as follows:

1. *Tertian*, characterized by a paroxysm every forty-eight hours; caused by *Plasmodium vivax*.

2. *Quartan*, characterized by a paroxysm every seventy-two hours; caused by *Plasmodium malariae*.

3. *Estivo-autumnal*, an irregular type caused by *Plasmodium falciparum*.

The first two types are known as the *regular intermittent types* and are characterized by paroxysms consisting of a chill and fever after which the temperature returns to normal and the patient is fairly comfortable until the next paroxysm. In the third or *remittent* type the fever varies in intensity, but the patient does not become afebrile as in the other types. This is the type which causes malaria to be a deadly and dreaded disease. It is often spoken of as pernicious malaria. Tertian malaria is the most common form; quartan is the least common.

Mode of Infection.—The different species of malaria parasites are closely related and are transmitted in the same manner—by the bite of a female mosquito of the genus *Anopheles*. Of this genus 12 or 15 species are capable of transmitting the infection under natural conditions. In malaria-infected countries many people become carriers; i.e., they harbor the parasites in their blood but do not exhibit symptoms of the disease. Carriers are of importance in the spread of malaria. Unrecognized infections and insufficient treatment lead to the carrier state.

Development of the Parasite in Man.—When young malaria parasites (sporozoites) are introduced into the blood stream, each one bores into a red blood cell and begins to

*A fourth recognized type of the parasite is *Plasmodium ovale* whose appearance and cycle are very much like those of *Plasmodium vivax*. Infection with this parasite usually produces mild symptoms. The parasite is not widely distributed over the world.

develop. When the parasite reaches maturity, it arranges itself in a number of segments. Suddenly the segments separate, the blood cell is destroyed, and each segment becomes a young parasite, known as a merozoite. This is known as *segmentation*. Some of the merozoites are destroyed by the blood plasma, but the majority bore into red blood cells where the process of growth and segmentation is repeated. In some cases two or even three or four parasites invade a single cell. The time elapsing between the entrance of a parasite into a blood cell and its segmentation is known as the *cycle* of the parasite. The cycle of *Plasmodium vivax* is forty-eight hours and of *Plasmodium malariae*, seventy-two hours. The cycle of *Plasmodium falciparum* is usually forty-eight hours, but it does not have the regularity that characterizes the cycle of the other parasites. A certain number of parasites do not undergo a cycle of development and segmentation but produce male and female sexual forms which undergo sexual development when taken into the body of the mosquito. Sexual forms do not appear in the blood until the infection has persisted for two or three weeks.

Development of the Parasite in the Mosquito.—When a female Anopheles mosquito bites an infected person and ingests male and female sexual parasites, a rather complicated sexual cycle begins in the stomach of the mosquito in which, first, the female parasite is fertilized by flagella-like structures that break off from the male parasite. The fertilized parasite bores into the stomach wall, becomes encysted, and divides into many small spindle-shaped parasites (sporozoites). The cyst then ruptures and the sporozoites are carried by the lymphatic system to the “poison gland” of the mosquito which is so constructed that the parasites are ejected when the mosquito bites.

Cause of Symptoms.—The paroxysms of chill and fever that occur in malaria are due to the liberation of toxins when the parasites rupture. Sharp paroxysms occur in tertian and quartan malaria because all of the parasites rupture at about the same time, i.e., every forty-eight or seventy-two hours. In estivo-autumnal infections some of the parasites rupture ahead of time and some rupture behind time, so that

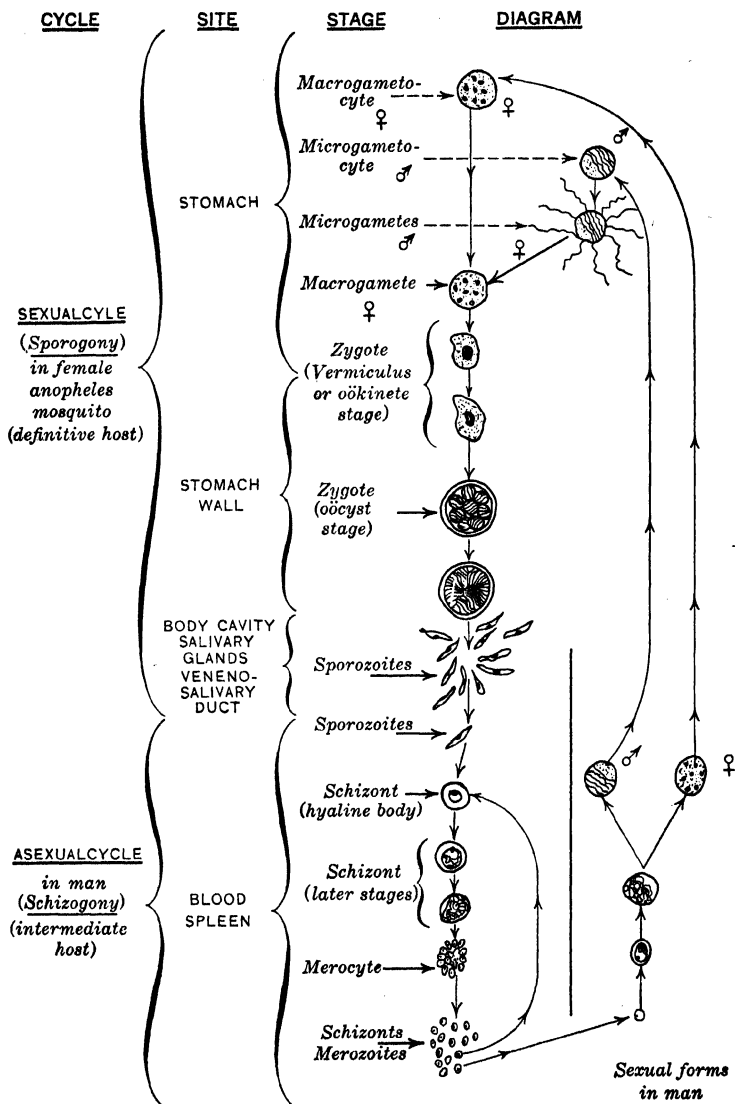


Fig. 108.—Development of the malaria parasite. (From Cummer: *Manual of Clinical Laboratory Methods*. Lea and Febiger.)

several hours are required for the whole brood to rupture. This explains why chills are usually absent and the fever is continuous in estivo-autumnal malaria. It is about two weeks after infection before enough parasites are present for their rupture to cause symptoms. This is the period of *incubation*.

Laboratory Diagnosis.—Malaria parasites may be easily seen in the red cells of properly prepared smears of the peripheral blood. Wright's and Giemsa's stains are most often used for staining the smears. The younger parasites appear as blue rings with a red chromatin dot attached to them, giving them a "signet ring" appearance. The quartan ring is thicker than the tertian and the estivo-autumnal ring is thin and hairlike. The latter often has two chromatin dots. Full-grown malaria parasites almost completely fill the cell and contain numerous red granules. Just before rupturing the parasites assume a segmented or rosette shape. The full-grown estivo-autumnal parasite is seldom seen in the peripheral blood. Malaria crescents are sausage-shaped parasites with a chromatin mass near their center. They are the sexual parasites of estivo-autumnal malaria and are frequently seen in the blood.

The laboratory diagnosis of malaria *does not consist of merely finding the parasites but includes the determination of their type*. This is of special importance when the blood of the patient is to be used in the treatment of paresis because the inoculation of a person with estivo-autumnal malaria may lead to most serious consequences. A small dose of quinine will drive the parasites out of the peripheral blood; therefore it is practically useless to examine the blood for malaria soon after quinine is given.

Immunity.—Repeated attacks of malaria seem to give the patient some resistance to the parasite. There is no true racial immunity to malaria. Mosquitoes, however, do not bite some people. This may be due to body odors.

Mosquitoes Transmitting Malaria.—Malaria is transmitted by various species of *Anopheles* mosquitoes. It is transmitted only by the female, because the male lives on fruits and vegetables instead of blood. Since the common house

PLATE VIII.—MALARIAL PARASITES

Plasmodium vivax (malaria tertiana)

- 1, 2. Ring forms.
- 3, 4. Early ameboid forms.
5. Double ring form.
6. Ring form.
- 7, 8, 9, 10. Ameboid forms.
11. Microgametocyte.
12. Macrogametocyte.
- 13, 14. Ameboid forms.
15. Ameboid form showing Schüffner punctation.
- 16, 17. Division forms.

Plasmodium malariae (malaria quartana)

- 18, 19. Ring forms.
- 20, 21, 22, 23, 24, 25, 26, 27. Ameboid forms showing malaria pigment.

28. Beginning division.
 29. Macrogametocyte.
 30. Ameboid form showing malaria pigment.
 31. Division form.
 32. Ameboid form showing malaria pigment.
- Plasmodium falciparum (malaria tropica)*
- 33, 34, 35, 36. Ring forms.
 37. Double rings.
 38. Section of brain capillary showing malaria pigment.
 39. Macrophage showing malaria pigment.
 40. Microgametocyte.
 41. Double rings.
 42. Macrogametocyte.
 43. Microgametocyte.
 44. Macrogametocyte.
 45. Multiple ring forms.

(From Gradwohl, *Clinical Laboratory Methods and Diagnosis*, The C. V. Mosby Co., St. Louis.)

mosquito (*Culex*) does not convey malaria, it is important to differentiate this mosquito from *Anopheles*. The *Culex* mosquito bites during the daytime; the *Anopheles* at night or about dusk. The wings of *Anopheles* are spotted while those of *Culex* are not. When *Culex* is resting on a wall its body is almost parallel to the wall while the body of *Anopheles* stands at an acute angle.

Prevention.—The prevention of malaria depends entirely on the prevention of the transfer of the infection from person to person by mosquitoes. Procedures which have this for their purpose are: (1) screening of houses, (2) prevention of breeding of mosquitoes by draining and oiling ponds and the use of minnows to destroy the larvae, (3) proper treatment of patients with antimalarial drugs, and (4) the detection and cure of carriers.

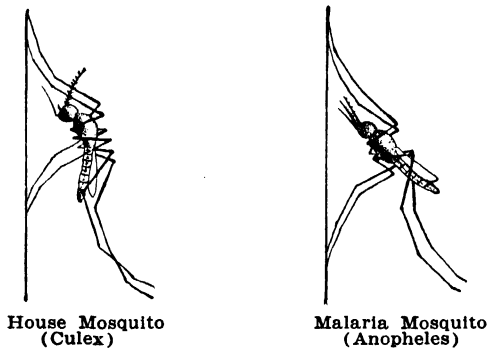


Fig. 109.—Drawing showing appearance of malaria and common house mosquitoes. Note that the body of the malaria mosquito is almost straight and is at an angle of about 45° to the surface on which it rests, while the body of the house mosquito is curved and is parallel with the surface on which it rests. (From Cummer: *Clinical Laboratory Methods*. Lea and Febiger.)

B. TRYPANOSOMIASIS

Trypanosomes are spindle-shaped protozoa of which there are many species that invade the blood of many different species of animals. They are found in the blood plasma, not within the cells. Infection with trypanosomes is known as *trypanosomiasis*.

The types of trypanosomiasis of importance to man are African trypanosomiasis or African sleeping sickness and South American trypanosomiasis or Chagas' disease.

African Trypanosomiasis.—African trypanosomiasis occurs in two forms: Gambian trypanosomiasis due to *T. gambiense* and Rhodesian trypanosomiasis due to *T. rhodesiense*. Each is transmitted by a species of the tsetse fly. The fly becomes infected by ingesting the blood of a person with the disease and the parasite undergoes a cycle of development in the body of the fly. When the parasites develop to a certain point, they invade the salivary glands of the fly from whence they are transferred to persons bitten.

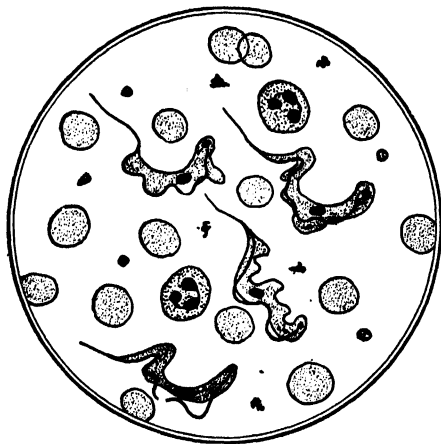


Fig. 110.—Blood smear showing trypanosomes. Note the relative size of leucocytes, erythrocytes, and trypanosomes. (From Rice: *Applied Bacteriology*. By permission of The Macmillan Co., publishers.)

Rhodesian trypanosomiasis is more virulent than the Gambian. Both diseases progress through stages of mental lethargy, stupor, and coma and usually end in death within ten months after infection.

South American Trypanosomiasis.—This type of trypanosomiasis is caused by *T. cruzi* which is transferred from man to man by a small cricket-like insect. Whether infection is due to the bite of the insect or contamination of the skin with feces is not known. South American trypanosomiasis differs from African trypanosomiasis in that in the former the parasites multiply in the tissues instead of in the blood. If the patient survives the acute attack the disease becomes chronic.

C. KALA-AZAR

(Visceral Leishmaniasis, Dumdum Fever)

This is an infectious disease characterized by long-continued fever, splenic enlargement, anemia, and loss of weight and strength. It is caused by *Leishmania donovani*, a protozoon that occurs as a small oval body in one stage of development and as an elongated and flagellated body in another. No cases other than those originating in other countries have been observed in the United States. The mode of transmission of the parasite from man to man is not a completely solved problem, but most observers believe that it is transmitted by the sand flea. Ninety per cent of untreated cases die within two years. With the advent of the antimony treatment the death rate has been reduced to about 10 per cent.

D. AMEBIASIS

The term *amebiasis* indicates an infection with *Endameba histolytica*. The disease occurs in two forms, acute amebiasis (amebic dysentery) characterized by an intense dysentery with bloody, mucus-filled stools and chronic or latent amebiasis characterized by vague intestinal disturbances, muscular aching, loss of weight, etc. In some cases of chronic amebiasis symptoms are absent. The chronic form of amebiasis is more common than the acute and is probably responsible for more ill health.

Endameba Histolytica.—*E. histolytica* exists in two forms: as vegetative amebas and as cysts. Vegetative *E. histolytica* are two or three times as broad as a red blood cell and possess a rather active type of ameboid motion. Viewed under the microscope the pseudopods characteristic of ameboid motion, an indistinct nucleus, and red blood cells within the cytoplasm of the ameba, are seen. Vegetative amebas are very susceptible to injurious agents and when exposed to deleterious influences are quickly destroyed; therefore they are of little importance, if any, in transmitting the disease from person to person. The cysts are smaller than vegetative amebas, are nonmotile, and are surrounded by a

resistant wall. It is by the cysts that the infection is transmitted from person to person. Approximately 10 per cent of people harbor the parasite.

Life History of *E. Histolytica*.—The discussion of the life cycle of *E. histolytica* will be begun with the cysts by which the disease is transmitted from person to person. After the cysts are passed in the feces, they remain capable of causing



Fig. 111.—*Endameba histolytica*. Two are seen in the center of the field. They contain many red blood cells. (Collection of Dr. F. M. Johns, Tulane Medical School.)

infection for several days if not subjected to such destructive influences as heat and drying. When the cysts are swallowed, they pass through the stomach unchanged and the "shells" are dissolved by the intestinal juices, most likely by those of the small intestine, and the vegetative forms of the parasite are liberated. The vegetative forms pass to the large intestine where they attack the intestinal wall and produce ulceration. The vegetative amebas mul-

tively in the ulcers and escape into the lumen of the intestine, and if a diarrhea is present they are swept out of the intestinal canal. If a diarrhea is not present, they multiply one or more times and become encysted. Encystment does not occur outside the body.

Source and Mode of Infection.—A study of the life history of *E. histolytica* reveals three evident facts: (1) infection can be acquired only by swallowing cysts, (2) the only source of infection is the feces of a person excreting cysts, and (3) acute cases are of little danger as sources of infection because the feces of patients with acute amebiasis contain only vegetative parasites which quickly die and could not survive the acid gastric juice should they accidentally survive long enough to be ingested. Infection is usually acquired by eating uncooked food contaminated by feces containing cysts. The most important single source of infection is the food handler with chronic amebiasis, especially the one engaged in the preparation of uncooked foods. Other sources of infection are vegetables fertilized with human excreta and drinking water contaminated with sewage. Apparently the latter was the cause of the Chicago epidemic of 1933. Flies and other insects may spread the cysts mechanically.

Lesions Produced by *E. Histolytica*.—In the majority of cases there seems to be a "state of balance" between the amebas and the host, in which the amebas are producing ulcers, escaping into the lumen of the intestine, and becoming encysted while the host is repairing the ulcers almost as fast as they are formed. In this case cysts are being excreted in the feces, and the patient experiences mild disturbances or none at all. This is chronic or latent amebiasis.

If the resistance of the host is lowered or a massive infection occurs, the host is not able to repair the ulcers as fast as formed and the increasing ulceration causes a violent dysentery in which the stools may consist entirely of blood and mucus. This is acute amebiasis or amebic dysentery. Occasionally intestinal perforation occurs.

On rare occasions amebas escape from the ulcers and enter the portal vein to be carried to the liver where they

produce an amebic hepatitis or liver abscess. In a few instances amebic abscesses occur in the lungs or brain.

Laboratory Diagnosis.—The procedures most often used in the laboratory diagnosis of amebiasis are the examination of *fresh warm* stools for vegetative amebas and the examination of ordinary specimens for cysts. Cultural methods and the examination of hematoxylin-stained specimens are of value. The complement fixation test devised by Craig is of value but the difficulty in obtaining a suitable antigen for the test restricts its general use.

Prevention.—The prevention of amebiasis depends on the proper control of carriers, proper sanitary supervision of foods and their preparation, and general cleanliness.

In addition to E. histolytica several other amebas may be found in the intestinal canal, but E. histolytica is the only one that causes disease.

E. INTESTINAL FLAGELLATES AND CILIATES

The most important intestinal flagellates are *Lamblia intestinalis*, *Trichomonas hominis*, and *Chilomastix mesnili*. Many protozoologists consider these parasites of little importance, but it is probably true that under certain conditions they cause mild digestive or nervous disturbances that are very resistant to treatment.

Balantidium coli is the most important intestinal ciliate. In some cases it seems to be a harmless inhabitant of the intestine, but it may invade the intestinal wall and produce an ulcerative colitis with an intense dysentery that may cause death. *Balantidium coli* is a normal inhabitant of the large intestine of the domestic hog. Man is probably infected by ingesting cysts passed by the hog.

F. VAGINAL TRICHOMONAS

(See page 725.)

Questions for Review

1. Discuss the process of nutrition by protozoa.
2. Discuss the development of the malaria parasite in man.
3. Discuss the development of the malaria parasite in the mosquito.

4. Give the length of time for each species of the malaria parasite to complete its cycle.
5. Give some differences in the Anopheles and Culex mosquito.
6. Discuss the prevention of malaria.
7. How is trypanosomiasis transmitted?
8. Give the clinical characteristics of the two forms of amebiasis.
9. Discuss the prevention of amebiasis.

True-False Test

Place the word "true" or "false" before each statement.

- 1. Protozoa are unicellular organisms and are the lowest form of animal life.
- 2. All protozoa are not motile.
- 3. Malaria is an acute febrile disease.
- 4. Carriers of malaria are never found.
- 5. The fever and chill that occur in malaria are due to the liberation of toxins when the parasites rupture.
- 6. Malaria parasites can be easily found after quinine has been given to the patient.
- 7. There is a racial immunity to malaria.
- 8. The vegetative amebas are responsible for transmitting the disease.

Completion Test

1. When protozoa are subjected to adverse conditions they become inactive and surround themselves with a resistant membrane, forming a -----.
2. According to the type of motility, protozoa may be classified into four groups: -----, -----, -----, and -----.
3. Three types of malaria are -----, -----, and -----.
4. Malaria parasites are transmitted by the bite of the ----- mosquito.
5. Blood of some malaria patients is used in the treatment of -----.
6. The infection with trypanosomes is known as -----.
7. The term amebiasis indicates an infection with -----.
8. Amebiasis occurs in two forms: ----- and -----.
9. List four facts that determine the source and mode of infection of amebiasis:
 1. -----
 2. -----
 3. -----
 4. -----

References

- White, E. Grace: General Biology, St. Louis, 1947, The C. V. Mosby Co.
- Craig and Faust: Clinical Parasitology, Philadelphia, 1945, Lea and Febiger.
- Strong, Richard P.: Stitt's Diagnosis, Prevention and Treatment of Tropical Diseases, Philadelphia, 1944, P. Blakiston's Son and Co.
- Albright and Gordon: Present Status of the Problem of Amebiasis, Arch. Int. Med. **79**: 253-271 (March), 1947.
- Chandler, Asa C.: Introduction to Parasitology, New York, 1944, John Wiley & Sons, Inc.

CHAPTER XXXV

RECOMMENDED METHODS OF INOCULATION TO PREVENT DISEASE*

I. Recommended Methods of the American Public Health Association†

A. Diphtheria.—1. Before the child is six months of age, immunization should be carried out by giving two injections of alum precipitated toxoid or three doses of ordinary toxoid at monthly intervals. All children under six years of age whose immunization has been neglected should be immunized in the same manner as infants. On entering school the child who was immunized in infancy should receive a single reinforcing dose.

2. Older children, and adults especially exposed to diphtheria such as nurses, physicians, and teachers should be immunized if they are found to be Schick positive. These persons should have preliminary “toxoid” tests. Those who do not show positive reactions are given toxoid and those who show positive reactions are given multiple small doses of diluted toxoid.

B. Pertussis (Whooping Cough).—Active immunization should be carried out not earlier than the third month, but before the sixth month.

C. Rabies.—Persons bitten by, or otherwise exposed to the saliva (through wounds, etc.) of rabid animals or animals suspected of having rabies (unless the animal is sub-

*In this chapter only the methods of inoculation recommended to prevent the more common and important diseases will be given. The student should consult original sources for the less commonly used methods. The methods given here are those primarily used to prevent the occurrence of the disease at some future time. The methods to be used when a person is exposed to a disease or is already ill of a disease which may be controlled by immunization are considered in only a few instances.

The methods given in this chapter may on occasion show a slight variation from those given in previous chapters of this book. This is because there is no complete uniformity of opinion among all authorizing agencies, public health workers, and physicians specializing in this field concerning the exact method which is most efficacious in bringing about an immunity in each condition.

†These methods are official with the United States Public Health Service, The United States Navy, and have been approved in principle by the Surgeon General, United States Army.

sequently proved not to have the disease) should have immediate antirabic treatment.

D. Scarlet Fever.—The Manual of Control of Communicable Disease merely states that an immunity can be brought about by administering scarlet fever toxin. The procedure is neither recommended nor condemned.

E. Smallpox.—Vaccinate children in early infancy and revaccinate on entering school or when the disease appears in a severe form. All persons who come in contact with a case of smallpox should be vaccinated.

F. Tetanus.—Immunization with tetanus toxoid in infancy or early childhood should be carried out in those areas in which there is a special danger of the disease. In addition to the toxoid used in the primary immunization, another dose should be given at the end of one year or upon receiving an injury which might be a source of tetanus. If no injury occurs, stimulating injections should be given at intervals of not more than five years.

G. Typhoid Fever.—It is recommended that the following groups of people be immunized against typhoid fever: (1) people who live in regions where typhoid fever is present, (2) people who by occupation or travel are subjected to unusual exposure, (3) all who have been exposed to a case of typhoid fever and those who may be exposed to a case, and (4) persons living in institutions where immunization may be carried out without difficulty.

II. Recommended Methods of the Committee on Therapeutic Procedures for Acute Infectious Diseases of the American Academy of Pediatrics

A. Diphtheria.—Children should be immunized between the ninth and twelfth month. If the child was not immunized at the proper time but is still less than ten years old, immunization should be carried out. Immunization should be brought about by the administration of three doses of alum precipitated toxoid (0.5 c.c., 1 c.c., and 1 c.c.) subcutaneously at intervals of two to three months. Ordinary toxoid may be used. Adults should be immunized if they follow occupations such as nursing, etc., in which the

probability of exposure is great. Because of the danger of reactions, the dose should be less than that of children. The recommended dose is 0.1 c.c., 0.2 c.c., and 0.5 c.c., subcutaneously at intervals of two to three months. If the patient experiences no reaction with these doses, an additional 1 c.c. may be given. Persons over ten years of age need not be immunized unless they give a positive Schick test. Tetanus toxoid may be combined with diphtheria toxoid.

B. Pertussis (Whooping Cough).—The following methods of immunizing are given:

1. Pertussis vaccine immunizing (Sauer), 15 billion per cubic centimeter. At intervals of three or four weeks, 1 c.c. and 2 c.c. are injected in the deltoid area of the left arm, and 3 c.c. are injected in the triceps area. The injections are given subcutaneously. The double strength vaccine is not recommended. In some localities the dosage and schedule differ from the ones given above.

2. Pertussis vaccine immunizing (Kendrick and Elding), 10 billion per cubic centimeter in four doses as follows: 1 c.c. (left biceps), 1.5 c.c. (right biceps), 1.5 c.c. (right triceps), 3 c.c. (1.5 c.c. in each deltoid).

3. Pertussis detoxified vaccine 1.5 to 2 c.c. subcutaneously every two or three days for 3 to 5 doses.

4. Alum precipitated pertussis vaccine (Harrison-Bell) 0.2 c.c., 0.3 c.c. and 0.5 c.c. every four to eight weeks.

5. Alum precipitated vaccine (Kendrick and Elding): three injections of 1 c.c. with an interval of one week between the first and second doses and four weeks between the second and third doses.

C. Scarlet Fever.—Immunize only under certain conditions such as children in orphanages, etc., and doctors, nurses and attendants in hospitals for contagious diseases. Immunization of the general population should not be attempted. If immunization is carried out, it should not be attempted before the child is twelve months of age and preferably after the eighteenth month.

D. Smallpox.—Vaccinate an unvaccinated person at any age. Between three and twelve months is the optional time.

Repeat at six and twelve years and during epidemics. Be certain that a potent vaccine is used.

E. Rabies.—Immunize man on exposure and animals to control epidemics.

F. Tetanus.—Give three injections (0.5 c.c., 1 c.c., and 1 c.c.) of toxoid subcutaneously every two to four weeks. A stimulating dose is given at the end of a year. The alum precipitated toxoid may be used and three doses of 1 c.c. each injected at intervals of three to six weeks. Observe the same precautions as with toxoid preparations and in older children.

G. Typhoid Fever.—Vaccine may be given any time after two years of age. It is given in any locality where typhoid is likely to occur and in any persons such as travelers where there is danger of exposure. The doses given are 0.5 c.c., 1 c.c., and 1 c.c. at intervals of five to ten days. The immunity probably lasts about two years.

III. United States Military Personnel

A. Upon entering the service the recruit is given the following:

1. *Smallpox Vaccine.*—Vaccination is done by the multiple puncture method. If no reaction follows the first vaccination, the vaccination is repeated at intervals of not more than ten days until a "take," accelerated reaction or reaction of immunity is obtained.

2. *Typhoid Triple Combined Vaccine*, in doses of 0.5 c.c., 1 c.c., and 1 c.c. subcutaneously every seven days. The U. S. Army allows an interval of twenty-eight days to elapse in some instances in order that tetanus toxoid may be given at the same time.

3. *Tetanus Toxoid.*—a. (Alum precipitated), two doses of 0.5 c.c. intramuscularly at intervals of not less than four nor more than eight weeks (U. S. Navy). b. Plain toxoid: Three doses of 1 c.c. each administered every three or four weeks (U. S. Army).

B. For these routine immunizations boosters of stimulating injections are given as follows:

1. *Smallpox Vaccine.*—The vaccination is repeated at intervals of three years in the United States and at intervals of

one year outside the United States. If vaccination has not been done within the preceding twelve months, it is repeated when a member of the military personnel is sent overseas. Vaccination is repeated upon exposure to smallpox.

2. *Tetanus Toxoid*, 0.5 c.c. at the end of one year and at the end of each four years thereafter (U. S. Navy). The U. S. Army does not give injections after the first year except in case of injuries which might be complicated by tetanus. Both Army and Navy recommend a reinforcing dose of toxoid when an immunized person receives an injury which might be complicated by tetanus. In the nonimmunized, tetanus antitoxin is given. The U. S. Navy gives a stimulating injection to personnel going overseas provided such has not been done within the last twelve months.

3. *Typhoid Vaccine*, 0.1 c.c. intradermally annually (U. S. Navy); 0.5 c.c. subcutaneous annually (U. S. Army). When going overseas the vaccination is repeated or a stimulating dose is given provided such has not been done in the last twelve months.

C. Upon transfer to endemic areas of disease members of the military personnel are immunized as follows:

1. *Upon embarkation for overseas duty*: yellow fever, epidemic typhus fever, and cholera. Stimulating doses are given as follows: yellow fever every four years; epidemic typhus, every six months or when there is danger of an outbreak; cholera, every four to six months or when there is danger of an outbreak.

2. *Upon special order or when there is increased danger of exposure*. (1) U. S. Navy; diphtheria, plague, Rocky Mountain spotted fever, Japanese "B" encephalitis, and influenza vaccine (by order of the Surgeon General). (2) U. S. Army; plague, influenza, diphtheria, scarlet fever, and Rocky Mountain spotted fever.

D. Action taken when a member of the military personnel is exposed to some communicable disease:

1. *Tetanus*.—If the person has not received tetanus toxoid, tetanus antitoxin is given. If he has had tetanus toxoid, a stimulating dose is given.

2. *Rabies*.—Rabies vaccine.

3. *Smallpox*.—Upon exposure or in the presence of an epidemic, revaccinate.

4. *Measles*.—Immune globulin in susceptible contacts under certain conditions (U. S. Army).

References

The American Public Health Association: The Control of Communicable Diseases (1945).

War Department Technical Bulletin (TB Med 114): Immunization (Nov. 1944).

American Academy of Pediatrics: Report of the Committee on Therapeutic Procedures for Acute Infectious Diseases and on Biologicals (1945).

Bureau of Medicine and Surgery, U. S. Navy: Personal communications from the Surgeon General.

PART II

PATHOLOGY

CHAPTER XXXVI

PATHOLOGY: DIVISIONS AND IMPORTANCE

The word pathology is derived from two Greek words, *pathos* meaning suffering or disease, and *logy* meaning science. Pathology is therefore the science of disease. It considers the cause of disease, how disease develops in the body, and the changes and final effects that it brings about in the body. It has for its purpose the correlation of the manifestations of disease with the underlying departures from normal that cause them. In short, pathology deals with all phases of disease except its treatment. Although not a part of pathology, the treatment of a disease cannot be successfully carried out without understanding the underlying body changes brought about by that disease.

If we may define *biology* as the science which treats of the normal origin, structure, and functional activities of an organism, *pathology* may then be defined as the science which treats of how the origin, structure, and functional activities of an organism are altered by abnormal influences. Pathology is based on four other sciences—*anatomy*, *physiology*, *chemistry*, and *physics*. It falls into several divisions. *Gross pathology* treats of the gross changes in structure which the body undergoes as a result of disease. *Microscopic pathology* (pathologic histology) treats of the changes in microscopic structure which cells, tissues, and organs undergo as a result of disease. *Functional pathology* (morbid physiology) treats of the changes in body functions brought about by disease. *Comparative pathology* has for its purpose the comparison of the diseases of the human body with those of lower animals. *Experimental pathology* is the study of artificially induced diseases.

General pathology deals with disease processes such as disturbances of circulation, inflammation, etc., which may

affect many tissues and organs or the body as a whole. *Special pathology* deals with the diseases of individual organs. *Surgical pathology* means the study of tissues removed at operation. *Clinical pathology* is a term embracing the various laboratory procedures used in the diagnosis of disease, such as urinalyses, blood examinations, cultures, smears, tissues, etc. It is a mistake to believe that *human pathology* (pathology of the human body) is the only kind of pathology. Just as important in the scheme of things as human pathology are *pathology of the lower animals* and *plant pathology*.

If a person knows the facts and principles of pathology applicable to the science and art of caring for the sick, that person is able to correlate the symptoms and signs of disease with the underlying changes that cause them, because *symptoms and signs are outward expressions of internal changes*. Such knowledge also enables one to bring into proper relationship seemingly unrelated manifestations of disease. This leads to correct diagnosis and gives an insight into the probable evolution of the disease, from which a prediction of its outcome (prognosis) can be made. A knowledge of the organ or organs primarily attacked by a certain disease enables medical attendants to carry out procedures that will lessen the burden on these organs. An acquaintance with the facts of pathology is necessary for the proper collection of specimens and the interpretation of laboratory reports. Both of these are of extreme importance because in some cases laboratory findings point more definitely to some particular disease than do clinical manifestations. If the material for examination is not properly collected or the reports are improperly interpreted, the net results may be not only worthless, but absolutely misleading.

Questions for Review

1. Define pathology.
2. Discuss the divisions of pathology.
3. Why does a nurse need to become acquainted with the facts of pathology?

References

Forbus, Wiley D.: *Reaction to Injury*, Baltimore, 1943, Williams & Wilkins Co.

CHAPTER XXXVII

THE HOSPITAL PATHOLOGIST AND HIS WORK

The activities of the department of pathology in a modern hospital fall into three divisions: *clinical pathology*, *surgical pathology*, and *autopsy pathology*. In a small hospital all three departments may be under the supervision of one pathologist. In a larger hospital each department may be under the supervision of a pathologist specially trained in the type of work done in that department. These pathologists may be aided by assistant pathologists. There are other workers known as *medical technologists* associated with each department. Medical technologists are not graduates in medicine but are educated in the basic sciences of physics, chemistry, and biology and had had special training in the technic of laboratory procedure. The pathologist himself not only is a doctor of medicine but he has had more than the usual training in general pathology and may have specialized in one or more of its branches.

I. The Clinical Pathologist

The person who, for want of a better name, is designated as a clinical pathologist is a person well versed in the performance of general laboratory procedures and their interpretation. He supervises such laboratory tests as urinalysis, blood counts, examination of sputum, gastric analysis, and chemical analysis of the blood. All bacteriological investigations and serological procedures, such as agglutination tests to detect the presence of the continued fevers, and complement fixation and precipitation tests to detect the presence of syphilis and certain other diseases, are under his control. Within his province are the skin tests to detect sensitization to the products of *Myco. tuberculosis* or the presence of an allergic state, undulant fever, susceptibility to diphtheria toxin, etc. In fact, he inherits all that the practice of pathology has to offer after the surgical pathologist and the autopsy pathologist have removed the parts peculiar to their

specialty. He is often consulted by the physicians practicing in the hospital. This honor he shares with the surgical pathologist and autopsy pathologist because it is just as important to know the nature of diseased tissue which has been removed from the body, or the cause of death, as it is to know about the results of cultures, the condition of the urine, or the chemical composition of the blood. This is as it should be, because the greater the cooperation between the physicians who have patients in the hospital and the pathologists, the better the patient's treatment.

II. The Surgical Pathologist

Although you may not see him in the operating room as often as you see the surgeon, the surgical pathologist in the better class hospitals takes a part in every operation in

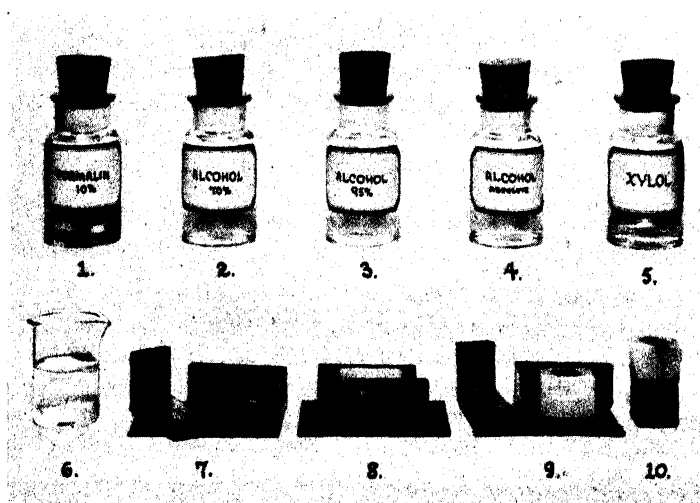


Fig. 112.—First step in the preparation of a tissue for examination; treatment to which tissue is subjected in order to cut it into sections (paraffin method). The block of tissue is first fixed in 10 per cent formalin (1) after which it is dehydrated by treating with alcohols of decreasing water content (2, 3, 4). The alcohol is then removed by xylol (5). This is necessary because paraffin is not soluble in alcohol and will not infiltrate the tissue if alcohol is present. After removing from xylol the tissue is kept in melted paraffin for several hours (6). An embedding box (7) is set up and filled with melted paraffin (8). The tissue is placed in the paraffin and the paraffin allowed to cool and harden. The embedding box is now dismantled and the tissue is securely held in a block of paraffin (9). The paraffin is then attached to a block of wood by melting the bottom of the paraffin (10) and the tissue is ready to cut. Note blocks of tissue in formalin.

which tissue is removed from the body, because this tissue is eventually subjected to his inspection and critical analysis. He has part of his equipment set up in the vicinity of the operating room where he may examine portions of removed tissue while an operation is in progress, to determine how the operation should be modified or completed. For instance, the operative procedure is quite different when a tumor of the breast or of any other part of the body is found to be malignant instead of benign.

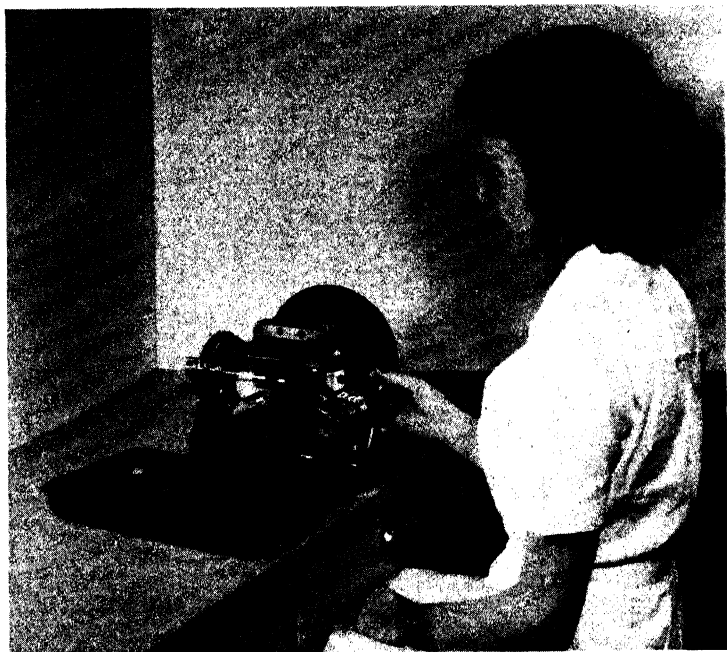


Fig. 113.—Second step in the preparation of a tissue for examination (paraffin method). The block of wood to which the paraffin-embedded tissue is attached is placed securely in the microtome. The technician then cuts thin sections of the tissue and floats them in a pan of warm water in order that they may be attached to slides.

It is quite interesting to understand what the surgical pathologist does with a portion of tissue removed from the body in order to determine with what type of disease it is affected, i.e., whether it is inflamed, the site of a tumor, or affected in some other manner, or whether, as occurs on rare occasions, it is a normal part erroneously removed. For

proper examination a portion of tissue must, immediately upon removal from the body, be put in some fluid which preserves the cells as nearly as possible in the state in which they were before they were removed from the body. This is known as *fixation*. One of the best fixing fluids is *formalin* (a solution of formaldehyde in water), which quickly penetrates the tissue and fixes the cells. The first step in the examination of the tissue is the *gross description*. In the gross

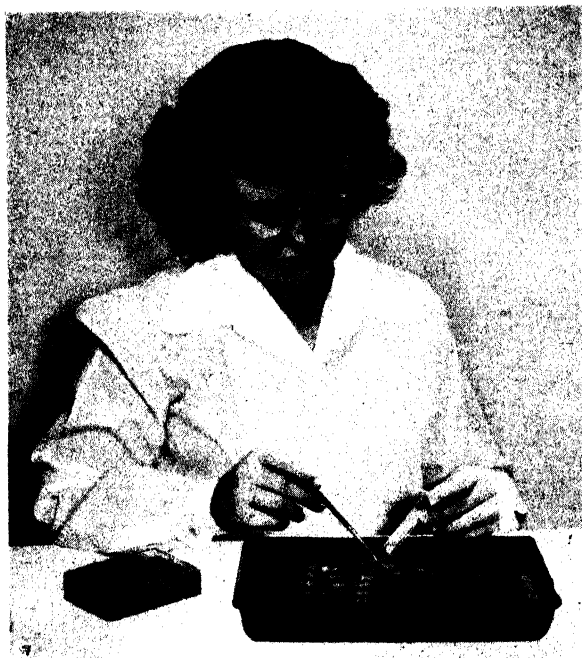


Fig. 114.—Third step in the preparation of a tissue for examination (paraffin method). Technician floating sections on slides. The top of the slide contains a thin layer of egg albumin and upon drying the sections of tissue are permanently attached to the slide and are ready to go through the staining process.

description the pathologist describes the tissue as it is received in the laboratory. In this description are included such characteristics as size, shape, weight, consistency, special markings, and appearance of cut surface. A deviation from normal, such as tumor formation, rupture of hollow organ, gangrene, the presence of an inflammatory exudate on the

surface or within the tissue, is noted. Lesions characteristic of some specific disease are carefully observed and described. At this time the pathologist removes small blocks of the tissue for sectioning. Needless to say, the portion of tissue from which the blocks are taken are carefully selected in order that all disease processes are included. After this, thin slices, which are known as *sections*, are cut from each block and examined by means of the microscope. This is known as the *microscopic description*. The sections are about 8 microns in



Fig. 115.—Fourth step in the preparation of a tissue for examination (paraffin method). Staining the sections. Note the different jars of reagent in which the sections are placed. As the sections are put through the different reagents, the paraffin is removed from the sections, the nuclei of the cells are stained blue (hematoxylin) and the cytoplasm pink (eosin). When the sections are stained, they are covered with a cover glass and are ready for microscopic examination. The technician is draining one reagent from the section before it is transferred to another reagent. Note the finished sections on rack.

thickness. Obviously, it would be impossible to cut such thin sections with an ordinary knife, and they are cut with a machine known as a *microtome*. Microtomes automatically advance the specimen the thickness of the section with each stroke of the knife so that section after section of the same thickness is cut. To cut sections of the same thickness, the

tissue must be thoroughly mobilized in the machine. One method is to embed the tissue in melted paraffin and to allow the paraffin to cool. The paraffin block containing the tissue is then placed in a rotary microtome and the sections are cut. Infrequently, the tissue is embedded in celloidin. In the other method the moistened tissue is placed on the table of a freezing microtome and carbon dioxide is allowed to enter the table and pass out through the perforations on the sides. This attaches the tissue to the table by freezing the water around the tissue, and the tissue is frozen at the same time, so that it is easily cut into sections.



Fig. 116.—Technician making sections with freezing microtome. Notice block of tissue on freezing chamber. After the tissue is frozen and the sections are cut, staining is carried out in the same general way as in the paraffin method. The preparation of tissues by the freezing method is used routinely in some laboratories. It is always used when a tissue is examined during the course of an operation.

After the sections have been cut and attached to a glass slide, they are stained. Staining makes the architecture of the tissue and the characteristics of the cells easily visible.

Most tissues are stained with two stains, one of which stains the nuclei while the other stains the cytoplasm. The most often used method of this type is the hematoxylin-eosin method, in which the tissue is first treated with hematoxylin

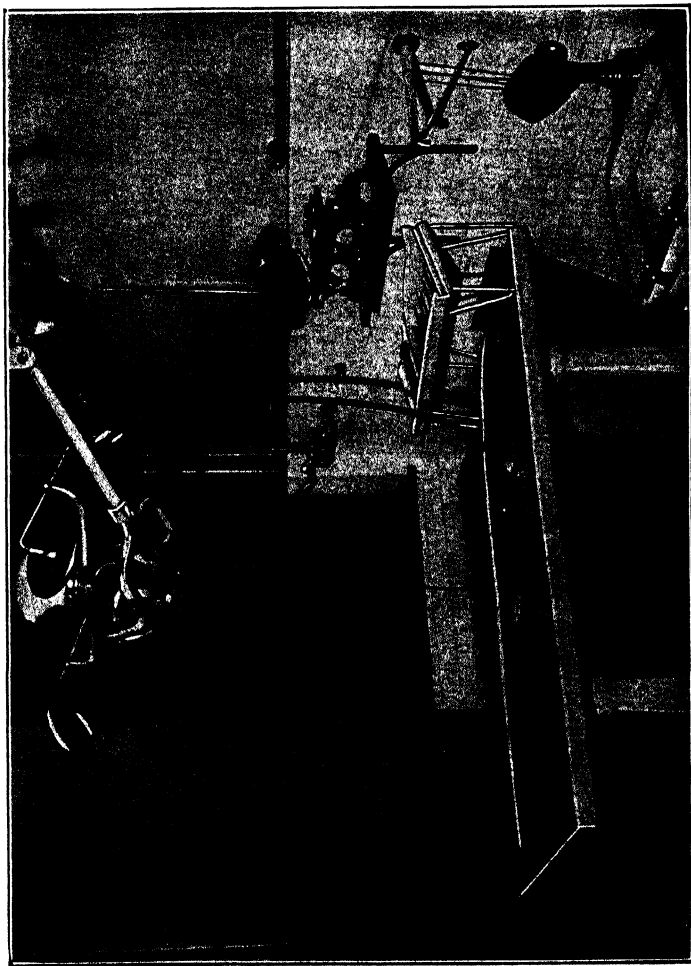


Fig. 117.—A portion of the autopsy room of the St. Louis County Hospital, St. Louis, Mo. Note overhead light and water supply, shelf for instruments and scales for weighing organs. (From Gradwohl: *Clinical Laboratory Methods and Diagnostics*. The C. V. Mosby Co.)

to stain the nuclei of the cells, after which it is treated with eosin to stain the cytoplasm. After the gross and microscopic descriptions are finished, the *diagnosis* is made. The pathologist should be furnished a complete history in all ob-

secure cases before he begins the examination of removed tissue. For this, there are more reasons than we can discuss here.

III: The Autopsy and the Autopsy Pathologist

In order that medicine may more closely approach an exact science, it is highly desirable that the correctness of the diagnosis be proved or disproved by autopsy in every case that ends fatally. So important is the autopsy in medical teaching that governing bodies refuse to recognize institutions that fail to secure a specified percentage of autopsies. Unfortunately, laymen, as a rule, do not understand the importance of autopsies or how they are performed, and consequently are adverse to the procedure. There are certain arguments in favor of the performing of autopsies with which those who are medically trained may approach the layman. Among these are: (1) if the correctness or incorrectness of the diagnosis is proved in a given case, the medical attendants in this case will be in a better position to render aid when subsequently a patient presents the same type of illness; (2) conditions or diseases that are of importance to surviving relatives may be discovered or, which is often as important, the surviving relatives may be comforted by finding that some disease they thought the deceased had was not present; (3) every person who has an autopsy done on his or her body, even in death makes a contribution to the science of medicine, to surviving relatives, and to those who will live in the future; (4) rare or new diseases are often discovered by the routine performing of autopsies; and (5) the autopsy yields important medical statistics and aids in the study of the hereditary characteristics of disease.

There are certain objections on the part of relatives of the deceased which are often met and must be answered with assurance. The first is that an autopsy is a ghastly and mutilating procedure to which one would hesitate to subject a member of his family. Those who constantly deal with death develop a respect for the dead body which probably is not possessed by those who do not have that training, and an autopsy performed by a capable pathologist leaves no more visible mutilation than an operation on the living performed

by a capable surgeon. After an autopsy has been performed, the body may be so completely restored to its original appearance that those who view the body will fail to recognize the fact that an autopsy has been done. A second objection is that a body upon which an autopsy has been done does not embalm well. This is not true if there is cooperation between the pathologist doing the autopsy and the mortician caring for the body. Several associations of morticians are now cooperating with medical societies in order to promote more autopsies.

Under present laws, an autopsy cannot be performed without permission from the next of kin of the deceased except in cases in which the detection of crime is an element. Some states permit an autopsy when the deceased requests it in his will. The permit should state whether the autopsy is to be complete or whether only certain parts of the body are to be examined. *It should be written.* The unauthorized performing of an autopsy is a cause for civil action and, in some states, is a violation of the criminal code.

In many hospitals it is the duty of the autopsy pathologist to teach interns, residents, and others how to approach the relatives of the deceased with a request for an autopsy, and by whom and when the results of the autopsy should be discussed with the relatives. Wherever this is done, more relatives will be tactfully approached, the results of the autopsy will be made known to them in a sympathetic and understanding manner, and the percentage of autopsies in that hospital will increase.

References

- Levinson, S. A., and Weller, M. C.: Obtaining Permission for Autopsy, *Am. J. Clin. Path.* 17: 834, 1947.
Warwick, Margaret: Obtaining Permissions for Autopsies, *Am. J. M. Sc.* 189: 341 (March), 1935.

CHAPTER XXXVIII

THE NATURE AND CAUSES OF DISEASE

I. THE NATURE OF DISEASE

In ancient times, disease was regarded as a punishment sent by the gods. As man's mind began to take a materialistic view of illness, he conceived the idea that the human body was made up of four liquors or humors—blood, phlegm, yellow bile, and black bile. What was considered "black bile" is not known. According to this idea, as long as these humors were in their proper proportion, the body enjoyed a state of health. When this proportion was disturbed, illness developed. This view held sway for a long time and was strengthened by the support it received from Hippocrates, later known as the "father of medicine." It was eventually superseded by the cellular concept of disease.

The Cellular Concept of Disease.—In 1847 Rudolf Virchow announced his concept of cellular pathology in which he held that all disease was brought about by changes primarily affecting the cells making up the body. This concept has withstood the test of scientific investigation, and the whole matter of disease can be summed up in accordance with this concept by saying that when all the cells making up a tissue or organ, except those destroyed by the natural wear and tear of life, are functioning in a normal manner, the tissue or organ is in a state of *health*. If more than this number are impaired in function, a state of *disease* exists. If these changes become so extensive that the tissue or organ is incapable of performing its functions in a normal manner, the *symptoms* of disease make their appearance.

What Disease Is.—Disease is an abnormal performance of certain physiological functions brought about by injury to the cells performing these functions. The symptoms and signs of disease are manifestations which arise from this abnormal performance of functions. Disease is not a stationary "thing" but a progressive series of changes which may end in recovery, permanent injury, or death. Accord-

ing to some workers, health is defined as that condition in which there is complete harmony between the organism and its environment both internal and external. Conversely, disease is that condition in which the organism is out of harmony with its environment either external or internal.

Structural and Functional Changes.—With abnormal activity of an organ, both structural and functional changes are often associated. It seems that some degree of functional change may occur without any marked change in structure but that most structural changes are associated with some change in function. In some conditions functional changes first call our attention to the presence of disease, and, if such conditions are corrected soon enough, detectable, structural changes may not occur. For instance, when some local cause which interferes with the venous outflow of blood from an organ or part is removed soon after the condition becomes apparent, the affected organ shows little, if any, change in structure, while if the cause is allowed to persist for a long time, the organ or part shows a marked increase in connective tissue and a reduction in the amount of functioning tissue.

The Interdependence of Organs.—When an organ becomes impaired to such an extent that it is not capable of functioning in a normal manner, other organs, or even the entire body, may become involved. For instance, when the heart becomes so impaired that it cannot pump sufficient blood through the body, the lungs become engorged and the amount of blood passing through them is lessened. This leads to decreased oxygenation of the blood (which normally occurs in the lungs), and the whole body suffers from oxygen want.

The Manifestations of Disease.—The changes produced in the tissues by disease are known as *lesions*. The diagnostic manifestations of disease are known as *symptoms*; symptoms may be subjective (those experienced by the patient but not apparent to an observer, such as pain and malaise) or objective (those which can be detected by an examiner, such as fever, swellings, paralysis, etc.). Objective symptoms are often called *signs*. A more or less sudden increase in the se-

verity of symptoms during the course of a disease is known as an *exacerbation*. An abatement of the severity of symptoms during the course of a disease is known as a *remission*.

Etiology and Pathogenesis of Disease.—By *etiology* is meant the cause of disease. By *pathogenesis* is meant the manner of development of a disease, that is, what its cause is, what changes it produces, and how it affects the structure and the functional activities of the involved organs and the body as a whole. Upon pathogenesis are based the prognosis and rational treatment of a disease.

Classification of Diseases.—An *acute* disease is one characterized by a swift onset and a rapid course. A *chronic* disease is one of slow evolution. A *communicable* disease is one that is transferred directly or indirectly from host to host. An *epidemic* disease is one that affects a large number of persons in a community in a short time. A *pandemic* disease is one that affects a large number of persons in many communities and countries at the same time. An *endemic* disease is one that is at all times present to a greater or less degree in a country. Congenital and hereditary diseases will be discussed under The Causes of Disease.

II. THE CAUSES OF DISEASE

The causes of disease may be variously classified. One classification divides causes into animate and inanimate. Another divides them into exogenous or extrinsic (arising outside the body) and endogenous or intrinsic (arising within the body). The classification which we will use in this book divides them into predisposing and immediate causes. The cause of a number of diseases is not known.

A. Predisposing Causes of Disease

Predisposing causes of disease are those causes which make the body more susceptible to the action of the direct causes. Among the important predisposing causes are the following:

Constitution.—By constitution is meant the sum total of those characteristics which determine whether a person will find it a difficult or an easy matter to exist in his environ-

ment. A person who is easily affected by adverse environmental condition is said to have a weak constitution, while one who is affected with difficulty by such conditions is said to have a strong constitution. How constitution plays its part we do not know. Constitution is largely hereditary, but it is modified to some extent by environment. It has no relation to muscular development because persons with highly developed muscles are just as likely to contract disease as those of asthenic build. An inherited constitutional predisposition to a disease is known as a *diathesis*; for instance, a hemorrhagic diathesis means an inherited tendency to have hemorrhages.

Age.—During intrauterine life the fetus may contract any one of a number of diseases incident to its antenatal residence, and it is exposed to the dangers of injury and infection as it passes through the birth canal. After birth, the infant may succumb to some condition that prevents the establishment of a normal extrauterine existence. Death during the first few days of life is often caused by conditions that existed during intrauterine life. Very young children enjoy an immunity to diseases that are very common in older children. This is brought about by the transfer of immune bodies from the mother to the child via the placenta. These antibodies disappear from the body of the child by the time it is six months old. Infants are susceptible to digestive disturbances resulting from improper food. Tuberculosis usually begins before the end of the third decade, while high blood pressure, heart disease, and kidney diseases usually occur after that time. Sarcomas, malignant tumors arising from connective tissue, are most common in young people, while carcinomas, malignant tumors arising from epithelium, are most common in older persons. Disturbances of nutrition and the manifestations of a number of diseases, especially diabetes, tuberculosis, and syphilis, differ in childhood and adult life. In old age, atrophic changes affect the different tissues and organs of the body and fibrotic changes occur in the heart and blood vessels.

Sex.—Men and women differ anatomically, physiologically, emotionally, and constitutionally. Many diseases are more

common in men than in women. Leaving out diseases of the reproductive system, few are more common in women. This seems to be due to an inherent increased susceptibility to disease on the part of males. In addition to this, because of occupation and exposure, men often contract diseases that are uncommon in women. General paresis, tabes dorsalis, cirrhosis of the liver, and high blood pressure are more common in men. Gallstones, hyperthyroidism, and nonsyphilitic heart lesions occur more often in women. Women withstand excessive blood loss better than men.

Race.—There is a difference in racial ability to live in different surroundings and in racial susceptibility and resistance to disease. Some races live with ease in arctic regions and others thrive equally well in torrid climates, but the majority live better in temperate zones. The Negro is very susceptible to tuberculosis but very resistant to malaria and yellow fever. He has generalized syphilis more often than the white man, but his central nervous system is seldom involved. The American Indian is peculiarly susceptible to tuberculosis, while the Jew is said to be resistant to tuberculosis. Sick cell anemia is a disease of the blood that appears to be strictly confined to those of Negro extraction.

Food Supply and Nutrition.—The continued sustenance on food that is insufficient in quantity or quality leads to loss of weight and increased susceptibility to disease. A diet insufficient in certain constituents leads to the group of diseases known as *deficiency diseases*. Important among these are pellagra (due to a lack of nicotinic acid), beriberi (due to a lack of vitamin B₁), scurvy (due to a lack of vitamin C), rickets (due in part to a lack of vitamin D), and certain hemorrhagic diseases (due to a lack of vitamin K). Vitamin deficiencies are accompanied by increased susceptibility to infection.

A deficiency in calcium leads to faulty bone formation, increased nervous irritability, and increased pulse rate. A deficiency in iron leads to a certain type of anemia. Lack of iodine leads to simple goiter.

Overeating leads to fatty accumulations which interfere with the functional activities of vital organs and throw an extra burden on the circulatory system.

Alterations in metabolism may lead to the development of disease as exemplified in diabetes mellitus. The increased amount of sugar in the blood and tissues in this disease favors the occurrence of skin infections such as boils, caused by staphylococci and other organisms which grow especially well in the presence of sugar.

Living Conditions, Occupation, and Habits.—Living or working in dark, overcrowded, damp, poorly ventilated surroundings increases susceptibility to disease, and the same is true of overwork and those habits of life which cause continuous loss of sleep. The excessive use of tobacco or alcohol is an important predisposing cause of certain diseases.

Associated with occupation are the occupational diseases, such as lead poisoning among printers and painters, benzene poisoning among dry cleaners and manufacturers of rubber goods, tetra-ethyl lead poisoning among gasoline refiners, and radium poisoning among those who work with certain luminous paints.

Emotional Make-up.—Excessive emotional activity makes unusual demands upon the body and leads to exhaustion. That worry is the great killer is a saying based on a strong foundation of physiological fact.

Hereditary Factors.—It is essential that students have a clear conception of the difference between hereditary and congenital characteristics. The *inheritable* characteristics of an individual are the characteristics which he has received from his ancestors and which he will transmit to his offspring. Characteristics which are thus transmitted are body physique, color of hair and eyes, mental and emotional make-up, and expected length of life. Abnormal characteristics which are inheritable are color blindness, albinism, abnormal mental traits, hemophilia, a tendency to allergic conditions, increased susceptibility to certain drugs, and tendencies to such diseases as diabetes and gout. The Rh factor, an inherited characteristic of human blood, is probably responsible for many hitherto unexplained reactions following blood transfusion. It also is responsible for the anemia of infancy known as erythroblastosis fetalis. Defects, such as harelip, cleft palate, and spina bifida, which are due to

failure of parts to unite during intrauterine life, do not represent the transmission of specific characteristics but rather an inherited deficiency in developmental vigor. Inheritable characteristics do not necessarily appear in each succeeding generation but may appear in one generation and then skip several generations to reappear in another. These inherited traits are transmitted by blebs of protein material that reside within the chromosomes of the germ cells and are known as *genes*. Acquired conditions are not hereditary.

Congenital diseases are those which are acquired during intrauterine life but are not inherited in the true sense. Examples of congenital conditions are such diseases as syphilis and smallpox caused by the transmission of the infection from the mother via the placenta to the fetus in utero, and gonorrheal infections of the eyes (gonorrheal ophthalmia) acquired as the fetus passes through the birth canal. Much less often, gonorrheal infection of the eye may occur while the fetus is still within the uterus. Although caused by conditions which are inherited, the disease erythroblastosis fetalis must be considered a congenital but not an inherited disease.

Inbreeding causes an increase in the hereditary diseases in a family by increasing the chances of inheritance. In many cases, however, both parents must be affected before the disease is transmitted to the offspring. If no hereditary diseases are present in a family, inbreeding has little deleterious effect.

B. Immediate or Exciting Causes of Disease

The immediate, determining or exciting causes of disease are those which actually cause the disease. We shall now briefly discuss the most important immediate causes.

1. *Traumatism* (mechanical injury).—Under this heading are included blows, crushing injuries, cutting wounds, falls, damage produced by foreign bodies, the effects of pressure, etc. Local complications of many of these injuries are damage to important organs, hemorrhage, and infection.

With traumatism the condition known as shock is often associated. Shock is most frequently associated with massive hemorrhages, injuries of the abdominal viscera, extensive crushing injuries or prolonged surgical operations with considerable handling of the internal organs.

2. *Heat and Cold.*—Disease may result from exposure to a moderate increase in heat or cold over a considerable period of time or a shorter exposure to a much greater increase. In the first category belong frostbite, chilblains, etc., from exposure to cold, and heatstroke and sunstroke from exposure to heat; in the second, belong death from freezing, burns, and scalds. Cold depresses metabolism and retards cell reproduction. Burns are often complicated by shock and, if severe enough, may cause death within twenty-four hours. Causes of death at a later period are absorption of toxins from the burned area, bacterial infections of the area, and severe malnutrition. The healing of deep burns covering a considerable area is often followed by extensive scar formation with contraction and deformity of the part. Scars following burns are quite often the starting point of cancer.

3. *Changes in Atmospheric Pressure.*—Our bodies are accustomed to a certain atmospheric pressure, and any appreciable departure from that pressure, either above or below, gives rise to a distinct train of symptoms. Increased pressure causes disturbances in deep-sea divers and caisson workers. Symptoms do not occur as long as the increased pressure is sustained, but appear when the normal pressure is restored. The symptoms most frequently observed are hemorrhage and tearing of tissues. This is due to the expansion of the gases which have been absorbed from the blood in increased amounts by the tissues during the period of increased pressure. The occurrence of symptoms may be prevented by restoring the normal pressure gradually. This condition is known as “decompression sickness” and is referred to by deep-sea divers and caisson workers as “bends,” “chokes,” “itches,” and “staggers.”

Among aviators, mountain climbers, or those who are otherwise rather quickly transferred to an atmospheric pressure less than that to which they are accustomed, a train of

symptoms, consisting of rapid respiration, weakness, dizziness, nosebleed, and occasional vomiting, make their appearance. Where an altitude of 35,000 feet or more is reached, the aviator may suffer from "decompression sickness" which differs in no manner from that experienced by deep-sea divers and caisson workers. Decompression sickness at high altitude is independent of lack of oxygen.

4. *Insufficiency in Respiratory Air.*—Insufficiency in respiratory air may be due to changes in the surrounding atmosphere which produce a deficiency in oxygen or conditions of the respiratory tract itself, whereby air is prevented from entering the lungs. In drowning, water acts as a foreign body within the lungs. Death due to obstruction of the flow of air through the air passages is known as *strangulation*. *Asphyxia* is that condition in which the circulation continues after respiration has stopped.

People who live at high altitudes have an increased number of red blood cells, which compensates for the low oxygen content of the air by bringing more oxygen bearers (red blood cells) to the lungs to be aerated. When an altitude of more than three or four miles is reached, the oxygen content of the air is so low as to be incompatible with life.

5. *Electric Currents.*—There is no essential difference in the results of contact with natural and artificial electric currents. If death is not immediate, burns at the point of contact and shock are the usual findings. Immediate death is due to inhibition of respiration and circulation.

6. *X-rays and Radium.*—Slight exposure to x-rays or radium has no appreciable effect on the body cells; moderate exposures have a stimulating effect on the body cells, and heavier exposures destroy them. Young, actively growing cells are more susceptible to radiation (exposure to x-rays or radium) than are mature cells. This is the basis of the x-ray and radium treatment of cancer because cancer cells are not fully mature cells.

7. *Ultraviolet Rays.*—Long exposures to ultraviolet light may produce death of the tissues. An irritating exposure produces sunburn.

8. *Intoxication by Chemical Agents.*—The effects of chemical agents vary from slight local effects when affecting the body externally, to profound systemic effects when absorbed into the body. Chemicals and drugs producing the latter effect are known as poisons.

9. *Living Agents.*—Important among the living agents of disease are bacteria, fungi, protozoa, intestinal worms, and insects that live on the body or bring disease-producing agents to it. Together, the living agents are one of the most important causes of disease.

Questions for Review

1. When is a body said to be in a state of health?
2. Do structural changes occur without functional changes? Do functional changes occur without perceptible structural changes?
3. What is a lesion?
4. What is an acute disease? Chronic disease?
5. What are exacerbations? What are remissions?
6. Define disease.
7. What is a symptom?
8. What two things are based on pathogenesis?
9. What are predisposing causes of disease? Name some of the important ones.
10. Discuss the relation of occupation to disease. Name three occupational diseases.
11. Differentiate between congenital and hereditary diseases.
12. What are some of the immediate causes of disease? Give the symptoms which accompany a rapid decrease in atmospheric pressure.
13. Define: strangulation, asphyxia.

True-False Test

Place the word "true" or "false" before each statement.

- 1. Some diseases arise without cause.
- 2. General paresis is more prevalent among white people than among colored people.
- 3. Men and women are equally susceptible to all diseases.
- 4. Syphilis in the newborn is inherited.
- 5. A disease with which a person is born is always a hereditary disease.
- 6. In high altitudes the decrease in atmospheric pressure may act as a cause of disease.
- 7. Chilblains result from exposure to extreme cold over a long period of time.

- 8. Some races are more susceptible to certain diseases than are others.
- 9. If no hereditary diseases are present in a family, inbreeding has little deleterious effect.

References

- Karsner, Howard T.: Human Pathology, Philadelphia, 1942, J. B. Lippincott Co.
- Legge, Sir Thomas: Industrial Maladies, London, 1935, Oxford Univ. Press.
- Wiggers, Carl J.: Physiology in Health and in Diseases, Philadelphia, 1944, Lea & Febiger.
- Forbus, Wiley D.: Reaction to Injury, Baltimore, 1943, Williams & Wilkins Co.
- Moore, R. A.: Textbook of Pathology, Philadelphia, 1944, W. B. Saunders Co.
- Boyd, William: A Textbook of Pathology, Philadelphia, 1947, Lea & Febiger.

CHAPTER XXXIX

DEFENSES OF THE BODY AGAINST DISEASE

I. GENERAL CONSIDERATION

During his age-long struggle for existence, man developed a defense mechanism which enables him to overcome many agents of injury occurring in his environment. In the first place Nature provided him with special senses which act as watch dogs against danger, and the functional capacities of his vital organs are far beyond the demands of normal life. That we have much more liver, pancreas, adrenal gland, and parathyroid gland than we ordinarily use and we are able to lead a normal life after one kidney has been removed or after one lung has been rendered inactive by artificial collapse, are examples of the abundance of reserve tissue possessed by our vital organs.

Vital organs, such as the brain, heart, and lungs, are enclosed within bony cases and their surfaces are bathed with a watery fluid. The fluid surrounding the brain serves as a water bed to prevent undue jarring, and the fluid that bathes the surface of the heart and lungs acts as a lubricant. The condensation of resistant cells at the surface of the skin offers a barrier against physical and chemical injuries or bacterial invasion, and the same is true, to a less degree, of the mucous membrane lining the orifices opening upon the surface. It has been said that the body's first line of defense is its epithelium which covers the outside of the body and lines the cavities opening on the outside. In many cases the epithelium becomes thick at a site of irritation; ex., calluses.

The hairs in the anterior nares protect the respiratory tract by filtering bacteria and larger particles from the inspired air. The respiratory passages are lined with epithelial cells from the surface of which spring hairlike appendages, known as cilia, which sweep the overlying material from the deeper portion of the tract to the exterior of the body.

The blood supply of many parts of the body is protected by a series of anastomoses (connections) between the branches of the vessels supplying the part. In case a vessel is occluded, the blood is detoured around the obstruction by way of the anastomoses. This is known as the establishment of a collateral or compensatory circulation.

Closure of the glottis, during swallowing, prevents food from entering the respiratory tract. Coughing and sneezing serve the purpose of mechanically expelling irritating materials from the respiratory tract. In a similar manner vomiting and diarrhea mechanically rid the intestinal tract of irritating substances.

When the body becomes chilled, the superficial vessels of the skin contract to prevent heat from being carried to the surface for dissipation, and sweating stops so that cooling due to evaporation will be retarded. To aid in this conservation of heat the involuntary muscles of the skin contract, giving rise to "goose flesh." This is a futile reaction which is of value only in animals having hair or feathers, in which case the hair or feathers are raised to inclose in their meshes a thick layer of air which is a poor conductor. The muscular action associated with rigor and shivering increases heat production. When the body becomes too hot, the superficial vessels dilate and sweating occurs. This brings more heat to the surface for dissipation and increases cooling by evaporation.

Body cavities opening on the surface are protected by secretions which wash away bacteria and foreign materials. Certain body fluids, such as saliva, gastric juice, and bile, exert an antiseptic action which reduces bacterial invasion. For instance the gastric juice destroys almost all important bacterial toxins except that of *Cl. botulinum*.

In some cases when an irritant gains access to the tissues, it is borne away by the lymph and deposited in the nearest lymph nodes. An example of this is the deposit of coal dust in the lymph nodes receiving the drainage from the lungs of those who live in coal-burning regions (anthracosis). In a similar manner bacteria or cells from a malignant tumor may be carried to the nodes receiving the

lymphatic drainage from the site of disease. Here the protective mechanism fails, because bacteria frequently and malignant cells practically always destroy the lymph nodes and spread to other parts of the body.

From major injuries, such as moving objects, man protects himself by batting the eyes and dodging or moving out of the zone of danger. While some of these acts are of a voluntary nature, they are executed in such a reflex manner that they may be considered protective mechanisms of Nature.

When an organ or part of the body has an increase in the amount of work it has to perform, its functioning tissue increases and the organ or part enlarges. This is known as *hypertrophy*. Hypertrophy will be discussed in a subsequent chapter.

II. IMMUNITY

(See Microbiology, page 189.)

III. PHAGOCYTOSIS

(See Microbiology, page 200.)

IV. FEVER

Fever is a condition, due to many causes, ranging from mechanical injury to bacterial infection, which is characterized by an increase in body temperature and destruction of body tissues. Of these causes bacterial infection is by far the most important. Although the manifestations of fever are disagreeable, its purposes are beneficial, because, if the temperature is not too high, it accelerates the destruction of bacteria or other injurious agents by increasing phagocytosis and by the production of immune bodies. The temperature of the body of warm blooded animals is rather closely controlled by the temperature regulating mechanism of the brain and is dependent upon two factors: *thermogenesis* (heat production) and *thermolysis* (heat dissipation). When the latter is decreased, the body temperature is raised. The latter is of much greater importance. In fever the temperature control mechanism of the body is set to give a higher

degree of heat in much the same manner as the temperature of an incubator is raised by adjusting the thermoregulator.

The temperature of man ranges from 98° to 99.5° F. (36.7° - 37.5° C.). Its variations depend on time of day, exercise, and age. It is usually lowest in the early morning hours and highest in the late afternoon. It is slightly higher in infants and children than in adults and is slightly lower in the aged. Alcohol and anesthetics may abolish the processes which regulate body temperature, thereby causing rapid chilling when the person is exposed to cold. Intoxicated persons have been known to have a body temperature of 75° F. A temperature of 107° to 109° F. causes profound disturbances of the brain cells.

There is a rather close relation existing between pulse rate and temperature. Ordinarily there is an increase of eight pulse beats for each 1.8° F. increase in temperature. Certain exceptions to this rule are of diagnostic significance; for instance, the pulse is comparatively rapid in tuberculosis, septicemia, diphtheria, and scarlet fever. In typhoid fever, meningitis, and yellow fever it is comparatively slow.

A *continued* fever is one in which the daily variation does not exceed 1.8° F. A *remittent* fever is one in which the daily variation exceeds 2° F., without reaching normal at any time. An *intermittent* fever is one in which periods of fever and normal or subnormal temperature alternate.

The course of a fever may be divided into three stages: (1) onset, (2) fastigium or acme, and (3) defervescence. During the stage of *onset* rigor and chill often occur. The superficial vessels of the skin are constricted and sweating is absent. This decreases heat loss and the temperature rapidly rises. The skin is pale and dry. The sensation of being cold is difficult to explain. It is more than likely due to a difference in the temperature of the deep and superficial tissues of the body. During the *fastigium* there is less need for reduction in heat loss. The superficial vessels dilate but sweating does not yet occur. This causes the skin to be flushed but dry. During the stage of *defervescence* marked sweating occurs. Heat loss exceeds heat production. As the temperature drops the normal hue of the body returns and

sweating ceases. Defervescence may be by *crisis*, in which the temperature returns to normal within twenty-four hours, or by *lysis* in which defervescence extends over several days, the temperature becoming a little lower each day until it returns to normal. Fevers which begin abruptly usually end by crisis.

Questions for Review

1. Name several mechanisms which serve to protect the body from disease or injury, and explain how each functions.
2. Discuss the protective action of the skin and mucous membrane.
3. How is the blood supply of many parts of the body protected?
4. What is the function of the hairs of the anterior nares? Of the nasal secretions?
5. What is the function of the ciliated epithelium which lines portions of the respiratory tract?
6. Explain how coughing, sneezing, vomiting, and diarrhea may serve as defensive mechanisms of the body.
7. Discuss the protective function of the lymph nodes.

True-False Test

Place the word "true" or "false" before each statement.

- 1. The normal structure and functions of the body in many instances serve to protect the body against injury.
- 2. The unbroken skin is a perfect protection against all bacteria.
- 3. The stomach is protected by acid gastric juice which kills many harmful bacteria.
- 4. Fever increases the activity of the phagocytes and antibodies and therefore is beneficial rather than harmful to the body.

References

- Forbus, Wiley D.: Reaction to Injury, Baltimore, 1943, Williams & Wilkins Co.
- Boyd, William: A Textbook of Pathology, Philadelphia, 1947, Lea & Febiger.

CHAPTER XL

DEGENERATIONS, INFILTRATIONS, PIGMENTATIONS, AND CONCRETIONS

Degenerations, infiltrations, pigmentations, atrophy, and necrosis (the last two will be discussed in subsequent chapters) make up the group of changes known as the *regressive** tissue changes. Necrosis (cell death) and tissue dissolution are the final outcome of the regressive changes, and some of the other regressive changes often are roads by which this end is approached. Frequently, the final outcome is not reached because the process becomes arrested at some point on the way and the cells and tissues return to their normal state. There are two major causes of regressive tissue changes, (a) action of injurious agents on the cells, and (b) reduction in blood supply to the cells. Later we will see that there is a group of changes which are by nature the opposite of the regressive tissue changes and that these changes are known as *progressive* tissue changes (see Chapter XLVI).

I. Degenerations

The degenerations are regressive tissue changes characterized by swelling of the cells and chemical changes within their cytoplasm which lead to the appearance within the cell of substances which are normally absent, present only to a slight degree, or invisible. The nucleus is not as greatly affected as the cytoplasm. The degeneration is named in accordance with the substance that appears in the cell. For instance, albuminous degeneration (cloudy swelling), etc. There are many causes of degeneration; important among these are microbial infections which may cause several different kinds of degenerations.

Cloudy Swelling.—Cloudy swelling is the most common and the least damaging of the regressive changes. It is a frequent accompaniment of diphtheria, typhoid fever, and pneumonia. Some degree of cloudy swelling occurs in practically all infectious diseases and follows extensive burns.

*Also known as retrograde or retrogressive tissue changes.

It may be found in inanition. The organs most often involved are the liver and kidneys. Less often the heart muscle is affected. Basically, cloudy swelling is caused by an increased water content of the cells. Affected cells are large and their cytoplasm has a cloudy appearance. Organs in which cloudy swelling occurs are large, pale, plump, and have the appearance of having been dipped in boiling water. They contain more water and coagulable protein than normal organs. As a rule, recovery is complete, but if the causative agent is especially severe in its action or persists for a long time, cloudy swelling may progress to fatty degeneration or necrosis.

A similar condition to cloudy swelling is *hydropic degeneration*, but in this condition the water content of the cell is so great that the water forms globules.

Fatty Degeneration.—See fatty metamorphosis.

Other Degenerations.—Among the remaining degenerations are (1) *hyaline degeneration*, which affects connective tissue cells and gives them a glasslike appearance; (2) *mucoid degeneration*, which affects the cells of certain tumors and causes them to swell up and become converted into a jelly-like substance; and (3) *colloid degeneration*, which occurs most often in cancers of the ovary and intestine. Boyd suggests that the term colloid as here used be abandoned because the material formed is not a true colloid (true colloid is found in the thyroid gland).

II. Infiltrations

Fatty Metamorphosis (Fatty Infiltration—Fatty Degeneration).—Books on pathology written only a few years ago made a distinct separation between fatty infiltration and fatty degeneration. It is now known that the difference between the two is not as great as it was once thought to be. By *fatty infiltration* is meant the deposit within the cells of fat that has been brought to them by the blood. The best example of fatty infiltration is the deposit of fat within (and between) the cells of the liver and heart in obesity. *Fatty degeneration* was formerly thought to be caused by the transformation of the cell material into fat. It is now believed that the process is a combination of infiltration and

degeneration as formerly understood, with the former playing the major role. It may follow cloudy swelling and may be present in metallic poisoning, prolonged fevers, and chronic diseases. The organs chiefly involved are the liver, kidneys, heart, and central nervous system. In mild cases recovery is complete. Prolonged and severe cases lead to cellular death. Since it is not always known exactly where the fat comes from in either condition, present-day treatises on pathology are inclined to consider both fatty infiltration and fatty degeneration under the noncommittal term, *fatty metamorphosis*.

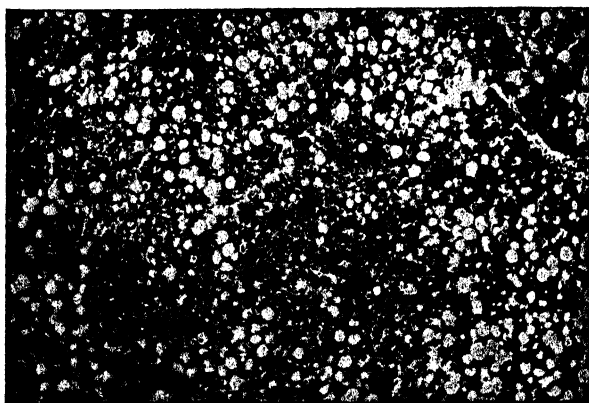


Fig. 118.—Fatty infiltration of liver. The fat appears as clear spaces.
(From Woolley: *Fundamentals of Pathology*. The C. V. Mosby Co.)

Amyloid Infiltration.—Amyloid infiltration is characterized by the deposit of amyloid, a waxy starchlike substance, in various organs, especially in the liver, spleen, and kidneys. It is an accompaniment of such long-continued suppurative conditions as tuberculosis and osteomyelitis.

Calcium Infiltration (Calcification).—*Calcification* is the deposit within the tissues of earthy salts without any attempt at bone formation. It is found most often in dead or dying tissues and may be an aftermath of various types of degeneration. Among the common examples of calcification are the calcification of tuberculous areas, the calcification of the blood vessels in arteriosclerosis, the calcification of degenerating tumors, and the formation of a calcified en-

velope around *Trichinella spiralis* in the tissues. A lithopedion or "stone child" is a retained fetus that has undergone calcification. Calcium metabolism is, to a great extent, under the control of the parathyroid glands and vitamin D.

Uratc Infiltration.—In gout, deposits of urates which are known as *tophi* (sing. *tophus*) occur in and about the joints, in the kidneys, and in the cartilage of the external ear. Occasionally, they are found in the eyelid. Because of the increased uric acid excretion at birth, extensive deposits of uric acid may be found in the renal tubules of the newborn infant. As a result of such diseases as pneumonia and leukemia a similar condition may be found in the adult.

Other Infiltration.—Other infiltrations which occur in rare instances are *cholesterol infiltration* and *glycogen infiltration*.

III. Pigmentations

The deposit of pigment in the tissues is not of infrequent occurrence. It may be brought about by a number of causes which have no other relation to each other. Abnormal pigmentation may result from an increase in amount or an irregularity in distribution of the normal pigments of the body (endogenous pigments) or the deposition within the tissues of pigments which gain access to the body from without (exogenous pigments) by way of the mouth, lungs, or skin.

The most important endogenous pigments are melanin, hemoglobin, and the hemoglobin derivative, bilirubin, which is of importance because it is the pigment that gives color to bile. Melanin is the normal coloring matter of the skin, choroid, and iris. In the skin it is found in the cells lying in the deeper layers of the epidermis. The more melanin present, the darker the complexion. Freckles are localized areas in which the melanin content of the skin is increased. Albinism is a congenital defect in which there is an absence of melanin from the skin choroid and iris. Pigmentated moles or *nevi* (sing. *nevus*) and the rapidly killing tumors known as malignant melanomas are tumors made up of melanin-containing cells. Icterus or jaundice is a yellow discoloration of the tissues caused by the retention of bile pigments within the body. It will be discussed in connection with diseases of the liver (page 679).

One of the best examples of exogenous pigmentation is the yellow discoloration of the skin which may follow the consumption of large amounts of carotin-containing foods (carrots, turnips, etc.). This condition (carotinemia) may be mistaken for jaundice.

When large amounts of dust are inhaled over long periods of time, a portion is deposited in the lung tissues and in the lymph nodes receiving their drainage from the lungs. This type of pigmentation is known as *pneumoconiosis*. The deposit of coal dust is known as *anthracosis*. The deposit of silicon dioxide is known as *silicosis*. This condition occurs in sand blasters, metal grinders, miners, etc., and is of importance because of the frequency with which it is complicated by pulmonary tuberculosis.

If silver salts are taken over a long period of time, the conjunctiva and skin may assume an ashen-gray color. This is caused by the deposit of silver albuminate in the superficial layers of the corium, just beneath the epithelium. This condition is called *argyria* and, once present, remains throughout the victim's life. Deposits of silver may occur in other parts of the body.

The formation of a blue line (known as a lead line) along the margins of the gums is one of the diagnostic features of chronic lead poisoning. It is much more noticeable in mouths that are not properly cared for and around decayed teeth. The line is brought about by a combination of the lead salts within the tissues and the hydrogen sulfide in the decaying material of the mouth. Similar lines are sometimes seen in chronic bismuth and mercury poisoning.

IV. Concretions

Concretions or concrements are solid masses formed within the passages or hollow organs of the body. The most important three, choleliths (gallstones), renal calculi (kidney stones), and vesical calculi (bladder stones) will be discussed in subsequent pages. Other concretions of importance are intestinal concretions, prostatic concretions, rhinoliths, salivary concretions, etc. Concretions are of importance because they may obstruct passages and act as a predisposing cause of infection.

Most concretions have a center or nucleus made of bacteria, cells, inspissated mucus, a foreign body, or similar material. The remainder of the concretion may be deposited around the nucleus in ringlike layers. The material deposited is derived from the medium surrounding the stone. Retention of secretions or excretions by pre-existing abnormality or disease is an important predisposing cause of concretions.

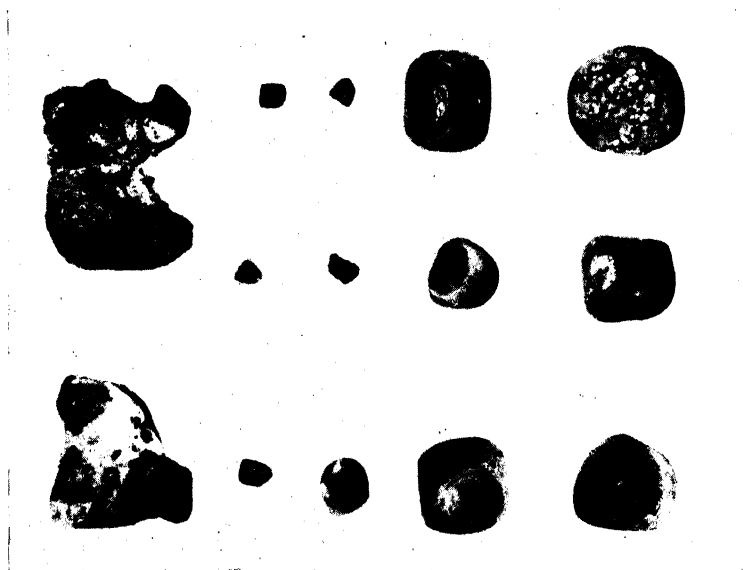


Fig. 119.—Concretions of various types. The concretions on the left are from the pelvis of the kidney. Those on the right are from the gall bladder.

The center of an *intestinal concretion* may be a foreign body, fruit stone, berry seed, an inspissated mass of feces, or a gallstone. The taking of large amounts of olive oil leads to the formation of fecal masses which may be mistaken for gallstones. Concretions composed almost entirely of feces may be found in the appendix.

Prostatic concretions are formed by the deposit of salts on corpora amylacea. Deposits of calcium in sebaceous cysts of skin give rise to cutaneous concretions. *Rhinoliths* are calculi formed in the nose. *Bronchioliths* are concretions formed

in the bronchi. A *pneumolith* is a stone which occurs in the substance of the lungs. Pneumoliths and bronchioliths are spoken of as "lung stones."

The taking of certain of the sulfonamide compounds is sometimes followed by the formation of sulfonamide concretions in the kidney tubules. This is more likely to occur in an acid than an alkaline urine.

Questions for Review

1. What are the regressive tissue changes?
2. What is the final outcome of regressive tissue changes?
3. Name the two major causes of regressive tissue changes?
4. Define and classify degenerations.
5. Describe the effects of cloudy swelling on cells and organs. What organs may be involved? As a frequent accompaniment of what diseases?
6. What is fatty degeneration? Fatty infiltration? Fatty metamorphosis?
7. What conditions or diseases are characterized by the various types of infiltrations?
8. Distinguish between endogenous and exogenous pigmentation. Give examples of each.
9. What organs of the body may be affected by concretions?
10. How do concretions differ from calcium infiltrations?
11. The taking of what drug may result in concretions in the kidney tubules? How may this be prevented?

References

- Anderson, W. A. D.: Synopsis of Pathology, St. Louis, 1946, The C. V. Mosby Co.
- Karsner, Howard T.: Human Pathology, Philadelphia, 1942, J. B. Lippincott Co.
- Boyd, William: A Textbook of Pathology, Philadelphia, 1947, Lea & Febiger.
- Moore, R. A.: Textbook of Pathology, Philadelphia, 1944, W. B. Saunders Co.
- Forbus, Wiley D.: Reaction to Injury, Baltimore, 1943, William & Wilkins Co.

CHAPTER XLI

NECROSIS, GANGRENE, AND SOMATIC DEATH

In the multicellular organism there are three recognized forms of death—necrosis, necrobiosis, and somatic death. By *necrosis* is meant the death of cells, tissues, or organs while yet a part of the body. *Necrobiosis* is the death of cells and their replacement by new cells as occurs in the normal processes of life (e.g., the shedding of the cells of the superficial layers of the skin and their replacement by normal cells). By *somatic or total body death* is meant death as ordinarily conceived, i.e., the cessation of all the ordinarily perceived activities associated with life. Widespread necrosis may occur without somatic death and necrobiosis is a constant accompaniment of normal life. At least a short time elapses after somatic death before cellular death is complete. Cellular death following somatic death is not a progressive simultaneous affair because the cells of some tissues die more rapidly than those of others.

I. Necrosis

Necrosis or death of cells, tissues, or organs, while yet a part of the body, may be caused by (1) mechanical injury, (2) interference with nutrition, (3) extremes of heat or cold, (4) chemical or bacterial poisons, and (5) nervous influences.

Necrotic foci may undergo liquefaction (liquefaction necrosis); they may be converted into a dry firm greenish mass (coagulation necrosis); or they may become converted into a cheesy material by the infiltration of fatlike substances (caseation necrosis). An example of liquefaction necrosis is the softening of the center of an abscess with the discharge of its contents. Coagulation necrosis is brought about by the coagulation of proteins. It is seen in infarcts, and it is this type of necrosis of the mucous membrane of the

stomach that occurs in carbolic acid and bichloride of mercury poisoning. Caseation necrosis is most often seen in tuberculous areas.

Necrosis due to the interruption of the blood supply to a part is of special importance. When the artery supplying an organ or part becomes occluded, the organ or part becomes necrotic provided it has no other source of blood supply. This is called *infarction* and the necrotic tissue is called an *infarct*. As a rule the infarct is conical in shape corresponding to the distribution of the artery and its branches. An artery may be occluded by embolism (see page 487), thrombosis (see page 484), disease of the arterial wall, or pressure on the vessel from without.

When a person lies in one position for a long time, the skin and subcutaneous tissues are compressed at the points of contact with the bed and their blood supply is interfered with. This leads to the formation of bed sores (decubitus) which are extremely painful and may lead to death.

II. Gangrene

The term "gangrene" is applied when a considerable mass of tissue undergoes necrosis and the part becomes the site of growth of saprophytic bacteria. It is classified as dry and moist gangrene. *Dry gangrene* is usually due to an interference with the arterial supply of a part without an interference with the return of venous blood from the part. Strictly speaking this condition is not a true gangrene but an infarction because bacterial growth plays an insignificant part or fails to occur at all. At the present time there is a tendency to refer to this condition as *ischemic necrosis*. On account of usage and the terms being ones that nurses will hear most often, we will use the terms dry and moist gangrene in this volume. *Moist gangrene* is primarily due to an interference with the venous return from a part, but the arterial supply is usually secondarily involved. Invasion by saprophytic organisms plays an important part in moist gangrene and is responsible for many of its prominent symptoms. Dry gangrene is confined almost entirely to the extremities, while moist gangrene may affect either extremi-

ties or internal organs. Gangrene of the internal organs may be caused by mechanical obstruction, compression by bands, twisting of pedicles, or thrombosis of terminal arteries brought about by lodgment of infected emboli from the heart.

In dry gangrene the part becomes dry and shrinks; the skin wrinkles, its color changes to a purplish brown or black, and complete mummification may result. The spread of dry gangrene is slow, and its symptoms are not so marked as those of moist gangrene. The irritation produced by the dead tissue causes a line of inflammatory reaction (line of demarcation) between the gangrenous area and the healthy tissue.



Fig. 120.—Dry gangrene of second toe. (From Hertzler and Chesky: *Surgery of a General Practice*. The C. V. Mosby Co.)

In some cases complete separation may occur along the line of demarcation. Lowered vitality, thickening of the vessel walls, and weakened circulation predispose to this type of gangrene. If bacteria invade the necrotic tissues and multiply, dry gangrene becomes converted into moist gangrene.

In moist gangrene the part is cold, swollen, and pulseless; the skin is moist, black, and under tension; blebs form on the surface; liquefaction occurs, and a foul odor (due to bacterial action) is present. The spread of moist gangrene is rapid; there is no line of demarcation between the normal

and diseased tissues; constitutional symptoms are severe, and death frequently occurs.

Senile gangrene is a special type of dry gangrene that occurs in the aged. It usually begins in the big toe where it may remain localized, or it may spread to the limb.

Diabetic gangrene begins in the same manner as senile gangrene but occurs in younger people. It extends upward more rapidly than a senile gangrene, and a line of demarcation is often absent. On account of the high sugar content of the tissues, which favors bacterial invasion, diabetic gangrene often becomes converted into the moist type.

Gas Gangrene.—See page 300.

III. Somatic Death

Vital Organs.—Those organs which are absolutely essential to the maintenance of life are known as *vital organs* and their relative importance is measured by the rapidity with which somatic death follows the complete cessation of their action. The sovereign triad of the vital organs is the central nervous system, the circulatory system, and the respiratory system. After complete obliteration of the central nervous system, death is almost instantaneous. Death usually follows within seven minutes after the arrest of either circulation or respiration. In both respiratory and circulatory failure the ultimate cause of death is lack of oxygen. Death follows within a few days after the removal of both kidneys, the liver or the pancreas. Removal of the stomach or spleen does not have any marked deleterious influence on health.

Signs of Death.—Usually there is a series of changes at death which makes its presence known to even the uninitiated observer, but occasionally it is difficult for an experienced observer to differentiate apparent from true death. Apparent death is most frequently seen in partial asphyxia, catalepsy, trance and syncope (fainting). It should be remembered that fainting is a dangerous condition which demands immediate treatment.

The criteria by which the presence of death may be determined are the *special signs of death* that occur with, or closely follow, the death struggle and certain cadaveric

changes that become apparent at a later period. The special signs of death are: (1) cessation of circulation, (2) cessation of respiration, (3) complete muscular relaxation and (4) eye changes. The presence or absence of heart action is determined by carefully feeling for the pulse and listening for heart sounds over a long period of time in absolutely quiet surroundings. In case of doubt, an artery may be opened. If the heart has not stopped there will be a gushing of blood. For some time after death the opening of a vein may be followed by a gush of blood. This is caused by postmortem contraction of the arteries which drives the blood into the veins and capillaries. The presence or absence of respiration may be detected by careful observation or by holding a mirror in front of the mouth and nose. If any air is being expired a fog will appear on the mirror. Peristaltic movement which sometimes continues after death should not be mistaken for respiration. As a general rule the heart continues to pulsate after respiration has ceased. An exception to this rule is death from an anesthetic. Complete muscular relaxation is an essential feature of death, but in cases where rigor mortis occurs at once, relaxation may not be detected. The eyes become glazed and this is especially noticeable at the canthi. Due to anemia and loss of muscular tone, the face usually but not always takes on the expression described as the *facies Hippocratica* characteristic of which are ashy pale skin, sunken eyes, thin prominent nose, pale thin lips and prominent chin and cheeks.

Cadaveric Changes.—The important cadaveric changes which follow death are (1) cooling of the body, (2) rigor mortis, (3) postmortem hypostasis and (4) signs of putrefaction. In some cases there may be a postmortem rise in temperature, but in any case cooling will eventually take place. The time of beginning and the rate at which cooling takes place are influenced by so many factors that no set rules can be given. Cooling is rapid for a short time and then proceeds more slowly until about twenty-four hours after death when the temperature of the surrounding air is reached. *Rigor mortis* (stiffening of the body after death) may occur almost

instantaneously when the person dies in a condition of great excitement, but as a rule it appears at some time during the first two hours after death and is complete within twelve hours after its onset. Rigor mortis first involves the muscles of the eyelids and jaws and then spreads from the head to the limbs. It lasts from twenty-four to thirty-six hours, leaving the body in the order in which it came and when broken up by mechanical means never returns.

Within one to six hours after death, dark red discolorations appear on the skin over dependent parts. These discolorations are known as *postmortem hypostases* or *livores mortis* and are due to the settling of blood into the capillaries and its diffusion into the tissues.

The first distinct putrefactive sign to be seen is a greenish discoloration of the abdomen caused by postmortem disintegration of the blood. Some organs are much more resistant to putrefaction than others. As a rule the brain succumbs first and the uterus last.

Time of Death.—While it is possible to arrive at an opinion as to the time a body has been dead, this is a matter for experts and should not be undertaken by the inexperienced.

Too Favorable Prognoses to Be Avoided.—I would warn against the habit of making too favorable prognoses, because we do not know what latent conditions lie smoldering in the body ready to be fanned into flames by the slightest departure from normal. People apparently in good health die suddenly for no discoverable reason. A strong man may die under an anesthetic or while having a trivial operation, while others may succumb to such emotional strains as joy, fear or anxiety.

Questions for Review

1. Which of the three forms of death occurs as a normal life process?
2. What condition may result in liquefaction necrosis? Coagulation necrosis? Caseation necrosis?
3. Compare moist and dry gangrene as to cause and symptoms.
4. What are some of the causes of gangrene of the internal organs?
5. Describe what is meant by *facies Hippocratica*.
6. Define rigor mortis. Describe its course.

True-False Test

- 1. Cellular death occurs simultaneously with somatic death.*
- 2. A bed sore is the result of gangrene of the tissue.
- 3. Diabetic gangrene is primarily a dry gangrene.
- 4. Dry gangrene spreads slowly and has a distinct line of demarcation between the normal and diseased tissues.
- 5. A gangrenous appendix is a dry gangrene.
- 6. The stomach is a vital organ.
- 7. As a general rule, pulsations of the heart continue for a short time after respirations have ceased.
- 8. Rigor mortis usually appears within two hours after death.

Completion Test

- 1. Interference with the arterial circulation results in ----- gangrene, and obstruction to the venous return of the blood causes a ----- gangrene.
- 2. Many symptoms of moist gangrene result from an invasion by ----- organisms.
- 3. In circulatory or respiratory failure the ultimate cause of death is lack of -----.
- 4. Special signs of death are:
 - 1. -----
 - 2. -----
 - 3. -----
 - 4. -----
- 5. The cadaveric changes following death are:
 - 1. -----
 - 2. -----
 - 3. -----
 - 4. -----

References

- Anderson, W. A. D.: Synopsis of Pathology, St. Louis, 1946, The C. V. Mosby Co.
- Boyd, William: A Textbook of Pathology, Philadelphia, 1947, Lea & Febiger.
- Karsner, Howard T.: Human Pathology, Philadelphia, 1942, J. B. Lippincott Co.
- Moore, R. A.: Textbook of Pathology, Philadelphia, 1944, W. B. Saunders Co.
- Gonzales, Vance, and Helpert: Legal Medicine and Toxicology, New York, 1940, D. Appleton-Century Co.
- Saphir, Otto: Autopsy Diagnosis and Technic, New York, 1946, Paul B. Hoeber, Inc.
- Gradwohl, R. B. H.: Clinical Laboratory Methods and Diagnosis, St. Louis, 1948, The C. V. Mosby Co.

CHAPTER XLII

DISTURBANCES OF CIRCULATION

The disturbances of circulation fall into two classes—general and local. Among the general disturbances are general passive hyperemia, edema, plethora (an excess of blood in the body), and oligemia (a deficiency in the volume of the blood). Among the local disturbances are active hyperemia, local passive hyperemia, ischemia, thrombosis, and embolism. Hemorrhage is of local occurrence but has far-reaching general effects.

I. Hyperemia

Hyperemia or congestion means an excess of blood in a part. It may be caused by an increase in the amount of blood brought to the part by the arteries or by an interference with the venous return of blood from the part. The former is known as *active* or arterial hyperemia and the latter is known as *passive* or venous hyperemia.

The excess of blood in a part that is the site of a hyperemia is contained in capillaries and arterioles or venules which have become dilated. Under normal conditions, not all the arterioles, capillaries, and venules of a tissue or organ are filled with blood, but many of them are empty and collapsed. When a hyperemia develops, they become dilated and filled with blood. In active hyperemia, dilatation is an act on the part of the vessels themselves; in passive hyperemia it is caused by an increased back pressure brought about by obstruction of the flow of blood through the veins.

Active Hyperemia.—Active hyperemia may be physiological or pathological. One purpose for which a physiological hyperemia is established is to supply an increased amount of nourishment to organs or tissues doing an increased amount of work. Active hyperemia initiates inflammation and forms one of its most important features. The site of an active hyperemia is red, swollen, and warmer than normal.

Passive Hyperemia.—In passive hyperemia the blood engorges the capillaries and some of its constituents escape into

the tissues because the veins do not properly remove the blood from the part. Passive hyperemia is always pathological and may occur as a localized or general condition.

The cause of a general passive hyperemia is most often an obstruction to the passage of blood through the heart; less often it is caused by an obstruction to the passage of the blood through the lungs. Among the causes of obstruction within the heart are mitral stenosis (the most important cause) and mitral incompetence. Among the causes of obstruction of the flow of the blood through the lungs are emphysema and pulmonary fibrosis. Local passive hyperemia results from the obstruction of a vein by (1) thrombosis or embolism, (2) thickening of the vessel walls, or (3) outside pressure upon a vein (neoplasms, contraction of scars, enlarged or misplaced organs, etc.). For a local passive hyperemia to occur the involved vessel must not possess a collateral circulation; i.e., it must not possess such communicating branches that the blood is shunted around the obstruction.

The site of a passive hyperemia is bluish red, swollen, and cold. The swelling is due to edema. If allowed to persist, passive hyperemia may lead to gangrene of the affected parts. Obstruction of the portal circulation leads to a widespread passive hyperemia characterized by dilatation of the veins of the abdominal wall and the hemorrhoidal veins (see hemorrhoids, page 674), ascites, and hemorrhages from the stomach and intestines.

In general venous hyperemia the amount of blood passing through the lungs is reduced; therefore, less of the blood in the body is oxygenated. This gives rise to dyspnea (shortness of breath), and the lips of the patient are cyanotic (blue) because unoxygenated blood has a bluish color. Edema of the lower extremities often accompanies general venous hyperemia.

In long-continued illnesses the heart often becomes weak and unable to maintain an adequate circulation, which causes the blood to sink to the dependent parts of the body. This is known as *hypostatic congestion*, and the dependent parts of the lungs and the skin of the back and buttocks are chiefly affected. In many cases hypostatic congestion can be prevented by frequently changing the position of the patient.

II. Local Anemia (Ischemia)

The term "local anemia" or "ischemia" refers to a lack of blood in a part which is caused by a reduction in the arterial supply of the part. This reduction may be caused by obstruction of an artery by (1) embolism or thrombosis, (2) external pressure, (3) thickening of the vessel wall, (4) nervous influences, or (5) the action of drugs or cold. For an ischemia to occur a collateral circulation must be lacking.

In ischemia the part is reduced in size, pale, cold, and functionally less active than normal. Persisting long enough, ischemia leads to necrosis. This condition, which is best seen in organs such as the spleen, kidney, and brain, in which the arteries do not freely communicate, is known as *infarction* (see page 474). Ischemia of the heart muscle and certain vital areas of the brain leads to immediate death.

III. Hemorrhage

Hemorrhage is an escape of blood from the vascular system as a result of a rupture of the heart or wall of a vessel (hemorrhage per rhexis) or the passage of red blood cells through the capillary walls without visible injury (hemorrhage per diapedesis).

The causes of hemorrhage are: (1) mechanical injury of the heart or vessels, (2) disease of their walls, (3) high blood pressure, and (4) diseases of the blood itself. The majority of brain hemorrhages and many of those occurring elsewhere are due to a combination of high blood pressure and disease of the vessel walls. Conjunctival hemorrhage may follow such violent efforts as coughing, sneezing, and vomiting. Cerebral hemorrhage of the newborn may arise from vascular disease or injuries from a long and difficult labor. Hemorrhages associated with primary diseases of the blood occur in pernicious anemia, purpura hemorrhagica, profound secondary anemia, and leucemia. In hemorrhage due to injury, clean cuts are followed by more loss of blood than crushing injuries or wounds produced by blunt in-

struments, because in the former arterial contraction is less effective and blood clotting material is less abundant in the wound.

The results of a hemorrhage depend on its location, the amount of blood lost, and whether the hemorrhage is sudden or gradual. When more than a third of the total blood is quickly lost, death usually occurs. Repeated small hemorrhages or the continuous oozing of blood lead to an anemia of greater or less severity.

Very small hemorrhages into the tissues are known as *petechiae*, larger ones are known as *ecchymoses*, and tumor-like collections of blood are known as *hematomas*. Hemorrhages also are named according to their location. For instance, *epistaxis* is nosebleed, *hemoptysis* is the spitting of blood, *hematemesis* is the vomiting of blood, *hematuria* is the presence of red blood cells in the urine, and *apoplexy* is hemorrhage within the cranial cavity.

When a vessel is opened and hemorrhage occurs, the hemorrhage is temporarily arrested by the formation of a blood clot in the opening (temporary clot). The presence of the clot excites an inflammatory reaction in the surrounding tissue, healing occurs in the manner described in the chapter on inflammation (page 494), and the clot is converted into a mass of fibrous tissue.

Hemorrhages occurring within twenty-four hours after an operation are usually due to a failure of the clotting process. Those occurring at about the tenth day are usually due to a softening of the clot by bacteria.

IV. Edema

A constant amount of fluid is maintained in the tissues by the nicely balanced relation existing between the passage of fluid from the capillaries to the tissue spaces and its removal from the tissue spaces by passing to the lymph channels or returning to the capillaries. When this balance is upset by increased passage, or decreased removal, an excessive amount of fluid accumulates in the tissues giving rise to the condition known as *edema*. Tissues which are the sites of edema are swollen, boggy, and doughy in consistency. When pressed

upon, they retain the imprint of the finger. This is known as "pitting" on pressure.

Anasarca is a generalized edema of the subcutaneous tissues. *Dropsy* is a collection of edema fluid in a body cavity. *Ascites* is dropsy of the abdominal cavity; *hydrothorax* is dropsy of the pleural cavity; *hydropericardium* is dropsy of the pericardial cavity. Collections of edema fluids in the tissues or body cavities are known as *transudates*. Similar collections of an inflammatory origin are known as *exudates*. Transudates and exudates may be differentiated by suitable laboratory tests.

The edema of heart disease begins in the feet and ankles and extends upward as cardiac embarrassment increases. The edema of kidney disease begins in the eyelids. Edema may interfere with circulation and cause difficulty in respiration. The patient with edema cannot rapidly regulate his blood volume because his tissues are so filled with fluid. Therefore, he is likely to suffer ill effects from an intravenous injection of a volume of fluid which could be taken with impunity by a normal person.

V. Thrombosis

Thrombosis is the formation of a mass, made up of one or more of the constituents of the blood, within the heart or blood vessels during life. The mass is known as a thrombus. Although coagulation may play an important part in thrombus formation, the process of thrombus formation and normal blood coagulation are quite different.

Factors of importance in thrombosis are: (1) injury to the lining of a blood vessel by traumatism, inflammation or degeneration, (2) slowing of the blood flow, (3) eddies in the blood stream, and (4) diseases of the blood itself. Of these the first is most important. Slowing of the current may be caused by enfeebled heart action, dilatation of a vessel or narrowing of a vessel. In narrowing, the current becomes slower as it approaches the constricted portion and in dilatation it becomes slower as it passes through the dilated portion. Thrombi may be composed of all the constituents of the blood in about their normal proportion, or they may be composed of one or more components with the exclusion of

the others, for instance, thrombi composed of platelets and fibrin or leucocytes and fibrin. Thrombi may be attached to one spot on the wall of a vessel and protrude into the vessel



Fig. 121.—Thrombus in vena cava. (From MacCallum: *A Textbook of Pathology*, W. B. Saunders Co.)

for only a short distance, leaving a passageway for the blood (parietal thrombi), or they may completely occlude the vessel (obstructive thrombi).

The most common sites of thrombus formation are the veins and heart valves. When thrombosis of an artery does occur, the cerebral arteries, thoracic aorta, or coronary arteries are most likely to be affected. The sudden appearance of a hemorrhoid is usually due to the formation of a thrombus in a varicose hemorrhoidal vein.



Fig. 122.—An organized and canalized thrombus. The wavy black line is a part of the vessel wall. (From Anderson: Synopsis of Pathology.)

The local effects of arterial thrombosis are the same as those of a noninfected embolism. Venous thrombosis, without the establishment of a collateral circulation, leads to passive congestion and gangrene.

The final effects of thrombi in order of danger to life are: (1) simple digestion, (2) organization, (3) formation

of nonseptic emboli, and (4) septic softening. Usually no ill effects follow simple digestion. Sometimes a thrombus undergoes organization and in some of these cases some of the capillaries taking part in the organization dilate to form canals through which the blood passes. This is known as *canalization*. The sequelae of the formation of nonseptic emboli are the same as those of nonseptic emboli due to other causes. When septic softening occurs, infected emboli are spread to different parts of the body with the usual results.

Massage of a thrombosed vessel, in order to relieve pain, is to be avoided because the thrombus may become detached, with most disastrous results.

VI. Embolism

By *embolism* is meant the obstruction of a vessel by some object floating in the blood stream. The object is known as an *embolus*. The source of an embolus is most often the left side of the heart (in endocarditis) or the veins.

Emboli may consist of portions of thrombi, portions of heart valves, clumps of fibrin from diseased heart valves, atheromatous material from a vessel wall, agglutinated bacteria, tumor cells, air, fat, animal parasites, or foreign bodies, such as shot, etc. Emboli may be sterile or contain bacteria.

The causes of embolism are diseases of the heart valves or blood vessels. It may follow injuries or operations or it may be associated with certain systemic diseases. In its course along a vessel an embolus may be arrested by division of the vessel, narrowing of the vessel, or by projecting points. The point at which arrest will occur depends on the place of origin of the embolus. Emboli arising in the systemic veins or right heart are usually arrested in the lungs and those arising in the left heart and aorta are usually arrested in the systemic circulation. The results of an embolism will depend on the nature of the embolus and the point of arrest. If a noninfected embolus lodges at a point supplied with a good collateral circulation no harmful results will follow. If there is no collateral circulation, ischemia of the part occurs and necrosis may follow (see Infarction, page 474). Emboli of pathogenic bacteria set up secondary foci of infection.

Emboli of tumor cells will set up secondary tumor growths. Embolism of the pulmonary artery, the coronary arteries, or vessels supplying vital areas of the brain may cause sudden death. Embolism of the arteries supplying the intestines leads to gangrene.

Fatty embolism is caused by fat entering the blood stream as a result of fractures of bones or blows which disturb the bone marrow, or operations or injuries that cause extensive disturbances of fat in any part of the body. The site of arrest is the lungs. The characteristic signs are oil droplets in the urine and the expectoration of an oily, frothy sputum.

Air embolism follows the opening of the large veins of the neck and thorax. Negative pressure produced by the inspiratory movements of the chest causes air to enter these vessels, and it passes to the heart where it mixes with the blood and is churned into a foamy mixture which the heart is unable to expel. A few cases of air embolism following the insufflation of the vagina during pregnancy have been reported. Postoperative emboli are due to the breaking away of thrombi at the site of operation.

Questions for Review

1. Classify the disturbances of circulation as to general and local involvement.
2. Differentiate between active and passive hyperemia.
3. What is a collateral circulation? What purpose does it serve?
4. What are the causes and symptoms of ischemia?
5. What are the common causes of hemorrhage?
6. Define: epistaxis, hemoptysis, hematemesis, hematuria, apoplexy, petechiae, ecchymosis, hematoma.
7. What is a "pitting" edema?
8. What are some conditions that may cause blood to clot in a blood vessel?
9. What is the difference between a thrombus and an embolus? Compare thrombi and emboli as to composition, causes, sites of formation, and possible results.

True-False Test

Place the word "true" or "false" before each statement:

- 1. Hyperemia means that there is more blood in the body than normal.
- 2. Passive hyperemia is a pathological condition due to interference with the return of venous blood from a part.

- 3. Under normal conditions, some of the arterioles, capillaries, and venules of a tissue or organ are empty and collapsed.
- 4. A weakness of the left ventricle of the heart will obstruct the flow of blood from the lungs to the heart, causing a passive congestion of the lungs.
- 5. An infarction may result from a local hyperemia.
- 6. General venous hyperemia gives rise to dyspnea and cyanosis.
- 7. Diapedesis is hemorrhage through the unbroken walls of the blood vessels.
- 8. Edema due to heart failure usually appears first around the eyes.
- 9. Edema associated with kidney diseases is more pronounced in the lower extremities.
- 10. Ascites is an accumulation of edema fluid in a serous cavity.
- 11. Thrombosis occurs more often in arteries than in veins.
- 12. The thrombosed vessel should be massaged to relieve pain.
- 13. Embolism is the clotting of blood within a vessel.
- 14. Embolism occurs only in the arteries and the portal veins.
- 15. Emboli formed in the left heart are usually arrested in the lungs.
- 16. Fatty emboli often follow a fracture of a long bone and usually lodge in the lungs.

References

- Anderson, W. A. D.: Synopsis of Pathology, St. Louis, 1946, The C. V. Mosby Co.
- Karsner, Howard T.: Human Pathology, Philadelphia, 1942, J. B. Lippincott Co.
- Forbus, Wiley D.: Reaction to Injury, Baltimore, 1943, Williams & Wilkins Co.
- Moore, R. A.: Textbook of Pathology, Philadelphia, 1944, W. B. Saunders Co.

CHAPTER XLIII

INFLAMMATION, REPAIR, AND REGENERATION

Inflammation is a local reaction of the tissues brought about by an injury. Within itself, inflammation is not a pathological condition but an exaggeration of physiological processes brought about by the presence of an irritant. The purpose of the inflammatory reaction is to destroy the agent producing the injury and to remove it, with the products of its action, from the body. Certain processes which have for their object the repair of the injury done and the restoration of the part to normal come into play almost with the beginning of the inflammatory reaction. These processes are so intimately associated with inflammation that workers consider them to be a definite part of it.

Causes of Inflammation.—The causes of inflammation are of two types: the living and the nonliving. The most important living cause of inflammation is bacterial infection. Less important living causes are microbes, other than bacteria, and animal parasites. The nonliving causes of inflammation may be classified as (1) physical (traumatism, extremes of heat or cold, electric currents, x-ray, radium etc.) and (2) chemical (acids, irritating gases, etc.).

The Inflammatory Exudate.—When an irritant gains access to the tissues and injures some of the cells, the capillaries and small vessels in the vicinity undergo a series of changes, the purpose of which is to surround the irritant with an *inflammatory exudate* as quickly as possible. The exudate consists of leucocytes, plasma (the liquid portion of the blood), fibrin, and red blood cells, all of which are derivatives of the blood, and wandering tissue cells which have been attracted to the site. As will be seen later, each of these elements, with the exception of the red blood cells, plays a specific part in the inflammatory process.

Depending upon the constituent that predominates, inflammatory exudates may be classified as serous, fibrinous, purulent, and hemorrhagic. A *serous* exudate is one composed

chiefly of the liquid portion of the blood. *Fibrinous* exudates are characterized by the presence of a large amount of fibrin. They occur most frequently on serous surfaces and often lead to adhesions. The purpose of these adhesions is to limit motion, seal perforations and restrain the distribution of bacteria and toxins. A *purulent* exudate is one composed chiefly of leucocytes or pus cells. Purulent exudates are most often caused by streptococci, staphylococci, pneumococci, meningococci, or gonococci. A *hemorrhagic* exudate is one containing many red blood cells. Hemorrhagic exudates usually indicate a grave condition. When there is considerable necrosis of the underlying tissues associated with a fibrinous exudate and many leucocytes, dead tissue cells, and bacteria are enmeshed among the threads of fibrin, the exudate is said to be *pseudomembranous*. A good example of this type of exudate is the pseudomembrane of diphtheria. Inflammations of mucous surfaces which are accompanied by a great outpouring of mucus, as in a "cold," are spoken of as **catarrhal** inflammations. In infectious processes the kind of bacteria causing the infection plays an important part in determining the nature of the exudate.

Kinds of Inflammation.—From the clinical standpoint inflammation may be classified as **acute** or **chronic**. An acute inflammation may become chronic or an inflammation may be chronic from the beginning. In chronic inflammation heat and redness are not so prominent as in acute inflammation. The polymorphonuclear leucocyte is the characteristic cell of the exudate in acute inflammation, while in chronic inflammation the cells of the exudate are chiefly lymphocytes or other mononuclear cells. Proliferation of the connective tissue cells in the vicinity of the inflammatory process is a prominent feature of chronic inflammation while it is negligible in acute inflammation. A *granulomatous* inflammation is one characterized by the formation of granulomas. A *localized* inflammation is one that is restricted to a small area, such as a boil or abscess. A *generalized* inflammation is one that is more widely distributed.

Local Changes in Inflammation.—We now attempt a brief description of the changes which occur when an irritant

gains access to the tissues and injures some of the cells thereby producing an acute inflammation, for instance, a staphylococcus infection of the finger. After a brief period of constriction, the small vessels and capillaries of the area dilate and become filled with blood, while the velocity of the blood current increases. The increase in the velocity of the blood that occurs with the dilatation of the small vessels is due to a more direct transmission of arterial pressure to these vessels. The velocity of the blood current now becomes slower. This is due to an increased viscosity of the blood and swelling of the endothelial cells lining the small vessels. Along with this the walls of the vessels have become more permeable to the cellular and liquid constituents of the blood. When the blood is flowing normally the red cells and leucocytes travel along in an axial stream surrounded by a zone of plasma, but when the current becomes slower the leucocytes fall into the plasma zone and adhere to the vessel wall. By their ameboid activity the polymorphonuclear leucocytes pass between the poorly cemented cells. Once outside the vessel, the polymorphonuclear leucocytes make their way along the tissue spaces toward the injurious agent. At the same time red blood cells, platelets, and plasma escape from the vessels. As the plasma escapes from the vessels fibrin formation occurs. The irritant is now surrounded by the inflammatory exudate, each component of which will play its own specific part in the ensuing battle. The polymorphonuclear leucocytes will remove bacteria, cellular debris, and solid particles by phagocytosis. The plasma (known as serum after fibrin has formed) will bring antibodies to the scene, dilute toxins which the bacteria have produced, and wash away bacteria and other foreign bodies. Wandering cells and certain leucocytes other than polymorphonuclears clear the ground for repair, and fibrin forms a restraining wall around bacteria and acts as a framework for the repair of the destroyed tissues.

Signs of Inflammation.—From ancient times we have been taught certain signs known as the cardinal signs of inflam-

mation. They are *redness* (rubor), *heat* (calor), *pain* (dolor), *swelling* (tumor), and *loss of function* (functio laesa).

Swelling of the inflamed area is due chiefly to the presence of the inflammatory exudate and, to a less extent, to the increase in the amount of blood in the part. Heat is due to the increase in amount of blood in the part and its increased rate of flow. Pain is caused by pressure and the action of toxic substances on sensory nerve endings. Disturbance of function may be due to pain, interference with nerve supply, limitation of muscle action brought about by the inflammatory exudate, or destruction of tissue.

Termination of the Inflammatory Process.—In a previous paragraph, we left the irritant surrounded by the inflammatory exudate. Subsequent events will depend on whether the protective powers of the exudate or the destructive activities of the injurious agent gain the ascendancy. If the exudate quickly overcomes the injurious agent, the rate of blood flow returns to normal; the normal caliber of the vessels is restored; the fluid of the exudate is absorbed; the fibrin, red blood cells, and dead tissue cells are removed by the leucocytes which, when their work is complete, enter the lymph stream leaving the part in its natural state. This type of repair is known as **resolution**. If the injurious agent gains the ascendancy, the process goes on to death of tissues with or without suppuration (pus formation). In addition to this the agent responsible for the inflammation may gain access to the lymphatics or blood stream and spread to distant parts of the body. In the average case, however, after the suppurative condition has progressed to a certain extent the defensive forces of the body again gain the ascendancy and healing follows. When suppuration occurs, the focus at first consists of a central mass of dead tissue cells, leucocytes, etc., surrounded by a zone of active leucocytes, wandering cells, and proliferating connective tissue. The surrounding leucocytes and wandering cells attempt to separate the dead tissue from the living; the dead tissue cells liberate ferments which have a destructive action on both themselves and the leucocytes, while the leucocytes produce ferments which liquefy the dead tissue cells. By this method

the central mass undergoes liquefaction. The liquefied material is known as *pus*. In acute inflammation the polymorphonuclear leucocyte is the chief element of pus. In chronic inflammation the lymphocyte or some other type of mononuclear cell is the chief element. In addition to these chief elements, dead tissue cells, red blood cells and, in bacterial infections, bacteria are present. The evacuation of pus is beneficial because it releases tension and removes dead cells and liquid portions of the exudate which have been rendered inactive, thus making room for a new and active exudate which the vascular system is ready to supply.

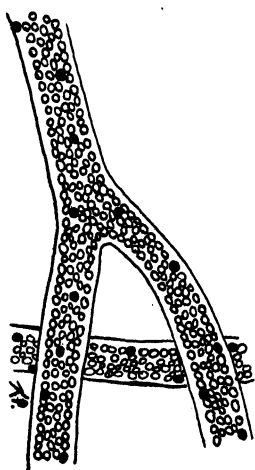


Fig. 123.

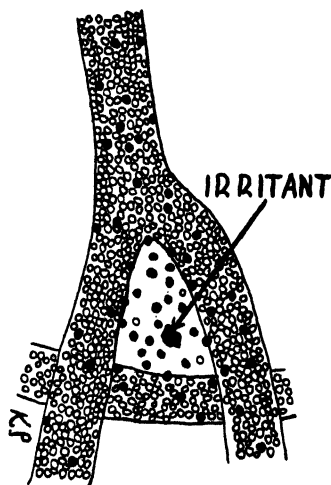


Fig. 124.

Fig. 123.—Diagram illustrating the normal blood flow. Note the blood cells in an axial stream separated from the vessel wall by a zone consisting chiefly of plasma. Leucocytes illustrated solid; red blood cells as circles.

Fig. 124.—Change in blood flow caused by the presence of an irritant. Note dilatation of vessels, increase in amount of blood in vessels, obliteration of the plasma zone and passage of the leucocytes through the vessel wall to surround the irritant. Leucocytes illustrated solid; red blood cells as circles.

Repair.—When the injurious agent has been overcome and dead tissue cells, dead leucocytes, and other casualties are being removed from the scene, reparative processes, though active before, assume the place of greatest prominence. If the walls of the injured area are not too far apart the gap is filled with elements of the exudate, chiefly plasma and interlacing strands of fibrin. Small capillaries grow into the



Fig. 125.—Scar of healed surgical incision through the abdominal wall.
(From MacCallum: *A Textbook of Pathology*. W. B. Saunders Co.)

fibrin, become filled with blood, and form a network between the walls. The connective tissue of the walls begins to proliferate and form young cells known as fibroblasts which grow into and completely replace the framework of fibrin which is absorbed. On account of its reddish granular appearance this youthful tissue, composed of capillaries and fibroblasts, is known as *granulation tissue*.* This method of repair is known as *primary union*. If the wound is so large that the gap cannot be filled with exudate, the capillaries grow into the exudate formed on the sides and

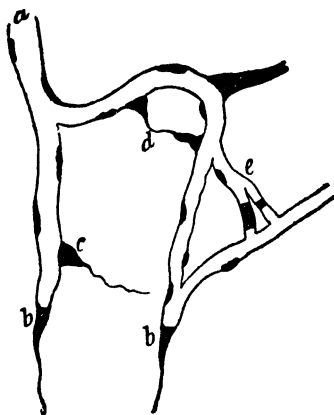


Fig. 126.—Formation of new capillaries. *a*, Capillary extending by means of terminal protoplasmic filament; *b*, *c* and *d*, Protoplasmic offshoots which will eventually form capillaries. *e*, Newly formed capillary. (From Woolley: Fundamentals of Pathology, The C. V. Mosby Co.)

bottom of the wound. Failing to find anchorage beyond the surface of the exudate the capillaries loop back on themselves. Fibroblasts proliferate as usual, and the exudate is converted into granulation tissue. The layers of granulation grow inward and upward until they fuse. This is known as *secondary union* and is most common in wounds complicated by bacterial infection.

When a certain point is reached in the healing of surface wounds by either primary or secondary union, the epithe-

*Granulation tissue is a very delicate tissue and it may be destroyed or its purpose defeated by too vigorous cleansing, too strong antiseptics, or too frequent dressing. Overtreatment, infection, or any unhealthy condition of the tissue may stimulate granulation tissue to such activity that it overfills the wound and protrudes beyond the surface as exuberant granulations or "proud flesh."

lium at the edges of the wound begins to proliferate and covers over the gap and, regardless of location or type of healing, when a certain point is reached the fibroblasts contract, the capillaries are absorbed and a white, bloodless glistening scar (cicatrix) remains. If a scab forms in the early part of the healing process it should not be removed because it protects the underlying epithelium.

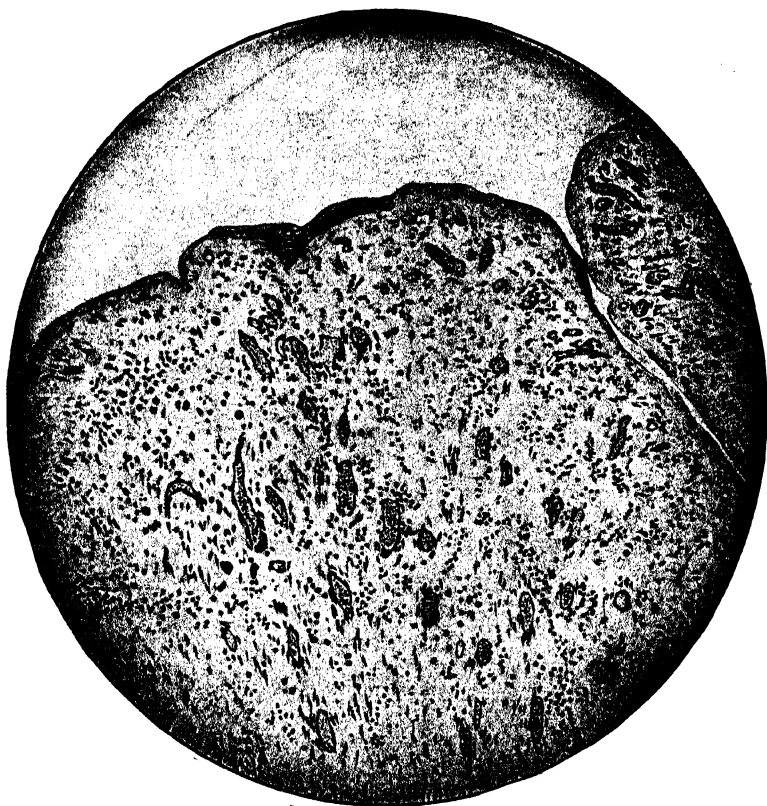


Fig. 127.—Granulation tissue formed in the healing of an ulcer. The granulation tissue has grown inward from both sides and is about to fuse. (From MacCallum: *A Textbook of Pathology*. W. B. Saunders Co.)

Inflammatory Lesions.—An *abscess* is a circumscribed focus of suppuration consisting of a central collection of pus surrounded by a wall of inflammatory tissue. If an abscess is located near the surface the presence of pus is indicated

by a yellow or green area on the surface near the center. As abscesses enlarge they attempt to open on a surface or into a cavity by extending ("pointing") in the line of least resistance. In this way they may travel great distances along muscle sheaths, etc. A good example of this is the psoas abscess (see page 752). Abscesses may reach the surface by the formation of narrow tracts known as *sinuses*. Sinuses become lined with granulation tissue but do not heal until the area which they drain has healed. A *phlegmon* is a noncircumscribed purulent infiltration of the tissues which spreads along fasciae and in spaces between muscles.

Boils or *furuncles* are abscesses located in the deeper layers of the skin and the subcutaneous tissue. Generalized boils are known as *furunculosis*. Boils and furunculosis often occur in persons who are poorly nourished and are frequently associated with diabetes. A *carbuncle* consists of several communicating boils draining through separate openings.

An *ulcer* is a circumscribed area of necrosis of the skin, mucous membrane or serous membrane, which is often, but not always, caused by infection. A tuberculous ulcer has thin undermined edges; a syphilitic ulcer has a punched-out appearance. A serpiginous ulcer is one that heals in one portion and spreads in another. An indolent ulcer has a dry appearance and exhibits little tendency to heal. A large and rapidly spreading ulcer is known as a *phagedena*.

A *fistula* is an inflammatory tract connecting a body cavity with the surface or one body cavity with another. Examples are fecal fistulas connecting the lumen of the intestine with the surface and vesicovaginal fistulas connecting the bladder and vagina. Fecal fistulas often follow resections of gangrenous portions of the intestines or the drainage of appendiceal abscesses. Vesicovaginal fistulas may be caused by injuries produced by instruments, long-continued pressure exerted by the fetus during childbirth, or by malignant growths.

Leucocytosis and Fever in Inflammation.—As an accompaniment of the inflammatory process there is often an increase in the number of leucocytes in the blood (leuco-

cytosis). This is due to the action on the bone marrow, which is an important site of leucocyte formation, of a factor formed at the site of inflammation. This factor is carried to the bone marrow by the blood. Many types of inflammation are accompanied by fever. This is due to toxic substances arising from the disintegration of bacteria and other cells in the inflammatory area.

Complications of Healing.—There are two conditions associated with the healing process that may be detrimental. They are the formation of permanent adhesions and the contraction of scars. Adhesions occur when two surfaces are in contact, and the healing process knits them together. This occurs most often in the pleural cavity where the visceral and parietal pleura become adherent (pleurisy with adhesions), in the pericardial cavity when the epicardium and pericardium become adherent (pericardial adhesions), and in the abdominal cavity where the omentum and coverings of the viscera form many different types of adhesions. Abdominal adhesions may lead to vague or distinct symptoms of discomfort, or, in extreme cases, they may cause intestinal obstruction. It should be remembered that in many cases the formation of permanent adhesions is due to the organization of fibrinous exudates whose beneficial purposes have already been indicated. Contraction of scars may limit the functions of various organs, cause strictures, and produce marked disfigurement. In some cases when a scar is kept tense it may stretch. This is one of the causes of postoperative hernia.

Chronic Inflammation.—Up to the present we have studied acute inflammation and should we now study chronic inflammation we would find that, although the clinical and microscopic pictures of the two conditions are quite different, the basic principles are alike. In both types exudation from the blood vessels and proliferation of certain surrounding tissue elements are found. In acute inflammation the formation of an inflammatory exudate plays the major role. In chronic inflammation proliferation of certain tissue elements plays the major role. For instance, in a boil much pus is formed but there is little proliferation of the surrounding

tissue, while in a chronically inflamed heart valve there is an increase in the amount of connective tissue with little cellular exudate.

Granulomatous Inflammation.—This type of inflammation is characterized by the formation of circumscribed growths known as *granulomas*. Among the diseases characterized by granuloma formation are tuberculosis, syphilis, leprosy, and certain other diseases. The granuloma characteristic of tuberculosis is the *tubercle*; of syphilis, the *gumma*; and of leprosy, the *leproma*. This granuloma formation is the only common characteristic of these diseases.

Reaction of the Tissues to a Foreign Body.—What disposal the tissues will make of a foreign body depends on the size and digestibility of the foreign body. If it is very small, like particles of soot, it is taken up by phagocytic cells and carried away. If the body is large, soft, and digestible it is invaded and digested by phagocytic cells. If it is large and solid but digestible it is surrounded by cells and gradually dissolved. If it is large but not digestible it becomes surrounded with cells that attempt to form a wall around it.

Regeneration.—The completeness of the restoration of destroyed tissue to normal depends on a number of factors, but the most important of these is the ability of the tissue to undergo regeneration, i.e., to reproduce tissue of its exact kind. Naturally, in a large wound several different kinds of tissues having different powers of regeneration are involved. The regeneration of cells destroyed by the natural wear and tear of life is known as *physiological regeneration*, while the regeneration of tissues destroyed by disease or some other type of injury is known as *pathological regeneration*. When tissues which have little or no regenerative capacity are destroyed, the defect is repaired by proliferation of Nature's omnipresent repair material—connective tissue. The same kind of repair usually takes place when there is *extensive* destruction of tissue having well-developed regenerative capacity.

The powers of regeneration, as a rule, are more highly developed in the lower forms of life; for instance, if an earthworm is severed, the result is two earthworms, and when

a newt loses a leg, another leg grows in its place. Regeneration is more active in childhood than in old age.

In man, epithelium, connective tissue, and capillaries regenerate with ease. Accessory skin structures (hair follicles, sweat glands, sebaceous glands) do not regenerate when destroyed. This is why scars are dry and hairless. If remnants of these structures remain, regeneration will take place. Periosteum and bone regenerate fairly well. Muscle regenerates poorly and wounds of muscle are usually repaired by the formation of scar tissue. Nerve cells never regenerate when destroyed, but their processes may regenerate provided the cell body has not been injured.

Questions for Review

1. Define inflammation. What are its purposes?
2. Classify the causes of inflammation.
3. What is the nature and purpose of the inflammatory exudate?
4. Classify and describe the different types of inflammatory exudates.
5. Describe in detail the changes which take place when a localized inflammation occurs.
6. What are the cardinal signs of inflammation?
7. What is the difference between chronic inflammation and acute inflammation?
8. What is pus? Why is the evacuation of pus beneficial?
9. What is granulation tissue? What are its functions?
10. Differentiate between primary and secondary union of wounds.
11. Explain the formation of scar tissue. Why is old scar tissue white?
12. What is an ulcer? Describe a tuberculous ulcer.
13. What are adhesions?
14. Why are scars hairless and dry?

True-False Test

Place the word "true" or "false" before each statement.

- 1. Inflammation is a protective mechanism.
- 2. All inflammations are due to some type of bacteria.
- 3. The power of white blood cells to destroy bacteria is known as leucocytosis.
- 4. The red blood cells are the most important cells in the inflammatory exudate.
- 5. An abscess is a localized collection of pus.
- 6. The presence of numerous boils is known as furunculosis.
- 7. An abscess of a hair-follicle is called a boil.
- 8. When repair follows inflammation without the formation of pus the process is known as resolution.

- 9. Inflammation accompanied by the formation of pus is known as suppuration.
- 10. When bacteria enter the tissues an exudate is formed around them.
- 11. Phagocytes are cells capable of destroying foreign bodies in the tissues.
- 12. In chronic inflammation the cells of the exudate are chiefly polymorphonuclear leucocytes.
- 13. Adhesions have a beneficial purpose to limit motion and prevent the spread of bacteria.
- 14. The evacuation of pus is beneficial; therefore it is advisable to remove pus from a boil by squeezing it.
- 15. "Proud flesh" is an overgrowth of granulation tissue which protrudes beyond the surface of a wound.
- 16. A fistula is an inflammatory tract which makes an abnormal opening between two hollow organs or between a hollow organ and the surface of the body.
- 17. If brain tissue is destroyed, it readily regenerates new cells to replace those which have been lost.
- 18. Connective tissue is often used in the body to repair tissue which has been destroyed.
- 19. In man, epithelium and muscle tissue regenerate most readily.
- 20. Reproduction of the same kind of tissues to replace that which has been destroyed is called regeneration.

Completion Test

In man ----- tissue, ----- tissue, and ----- regenerate readily, while ----- tissue regenerates poorly and ----- cells not at all.

References

- Karsner, Howard T.: Human Pathology, Philadelphia, 1942, J. B. Lippincott Co.
- Foot, N. Chandler: Pathology in Surgery, Philadelphia, 1945, J. B. Lippincott Co.
- Moore, R. A.: Textbook of Pathology, Philadelphia, 1944, W. B. Saunders Co.
- Boyd, William: Surgical Pathology, Philadelphia, 1947, W. B. Saunders Co.
- Rose and Carless: Manual of Surgery, New York, 1943, William Wood & Co.

CHAPTER XLIV

INFECTIOUS DISEASES*

I. GENERAL FEATURES

An infectious disease represents a combat between two living forces—the invader and the organism invaded. The invader may be bacterium, fungus, virus, Rickettsia, or animal parasite, and, in human pathology, the human body is the organism invaded. Since variability is a characteristic of things that live, there is double reason why infectious diseases should show considerable variation from type in their course. What is meant by this, for instance, is that most cases of pneumonia are much alike and manifest a rather characteristic train of symptoms but occasionally a case of pneumonia occurs in which some of these symptoms are absent or uncommon symptoms are present. The same is true of typhoid fever, epidemic meningitis, measles, smallpox, typhus fever, malaria, and many other diseases. This is why the recognition of an infectious disease is sometimes a difficult diagnostic problem.

From the standpoint of action on the body the causative agents of infectious disease may be classified as those that attack the tissues generally and those that primarily attack a single organ or system. Examples of the former are the causative agents of diphtheria and typhus fever. Examples of the latter are the bacillus of typhoid fever, which primarily attacks the intestinal tract, and the pneumococcus, which primarily attacks the lungs. In infections in which the attack is directed primarily to a single organ, it is not the effects of the organisms on the part attacked alone that causes illness or death but a general intoxication or injury to vital areas.

The course of most infectious diseases falls into several different periods; namely, (1) period of incubation,

*In this chapter only the most important pathological features of some of the more important infectious diseases will be considered. For a discussion of the causative agent and mode of infection in these as well as infectious diseases not included in this chapter the student is referred to the portion of this book devoted to Microbiology. Further consideration of these diseases will sometimes be included in the discussion of the special diseases of different organs and systems.

(2) period of prodromal symptoms, (3) period of invasion, (4) the fastigium or acme, and (5) period of decline. The *period of incubation* is the time elapsing between the time the infection was received and the appearance of symptoms. In some diseases its length is constant. In others it shows much variation. The *prodromal period* is a short period that sometimes follows the period of incubation and is characterized by the presence of such symptoms or headache, malaise, etc. The *period of invasion* is the period during which the disease reaches its full development. Invasion may be rapid (a few hours, as in pneumonia) or insidious (a few days, as in typhoid fever). The *fastigium* is the period during which the disease is at its height. Following this is the stage of defervescence, or decline, during which the symptoms subside. This may be by *crisis* (in a few hours) or by *lysis* (several days). During the stage of convalescence the patient regains his lost strength. Many diseases are *self-limited*, which means that under ordinary conditions of resistance on the part of the host and virulence on the part of the invading agent the disease will last a certain rather definite length of time and recovery will take place.

There are certain pathological changes which are found in nearly all infectious diseases, and in addition each infectious disease has its own peculiar pathological changes. Among the general pathological changes are some degree of anemia, cloudy swelling of different organs, an increase in lymphoid tissue, and digestive and nutritional disturbances. Practically all infectious diseases are accompanied by fever and many are accompanied by a leucocytosis (increase in white blood cells). If fever or leucocytosis fails to occur in infectious disease where they ordinarily occur, a grave condition is indicated.

II. DISEASES CAUSED BY STREPTOCOCCI

A. Scarlet Fever

Scarlet fever (scarlatina) is an acute infectious disease of childhood that is caused by a hemolytic streptococcus and is characterized by sore throat, severe constitutional symptoms, and a typical skin eruption with massive exfoliation.

Pathology.—The nasopharynx and tonsils may be covered with a membrane. The lymph nodes, especially those of the neck, are swollen and inflamed. The rash is due to an acute hyperemia of the skin with petechial hemorrhages. The blood count shows from 15,000 to 30,000 leucocytes, of which from 85 to 95 per cent are polymorphonuclears.

Complications.—Complications occur in about 40 per cent of cases of scarlet fever. A severe otitis media is one of the most common and is due to an extension of the organisms to the middle ear via the eustachian tube. Nephritis occurs in about 10 per cent of cases.

B. Acute Rheumatic Fever

Acute rheumatic fever is an acute infection that is probably due to a streptococcus. Some observers believe that it is an allergic reaction to streptococci. It is more common in the northern than in the southern states and is infrequent in the tropics. It seldom occurs in children less than three years of age and is most common between the sixth and twelfth year. Characteristic of the disease is the occurrence of small nodules in the connective tissue framework of the heart, serous and synovial membranes, subcutaneous tissue and brain.

So frequent are certain cardiac complications in rheumatic fever that they are often spoken of as rheumatic heart diseases. This is especially true of acute simple endocarditis. More than 50 per cent of attacks of rheumatic fever are preceded by tonsillitis, and there seems to be a direct causal relation existing between tonsillitis, acute rheumatic fever, acute simple endocarditis, and chorea. The prognosis in acute rheumatic fever is that of its cardiac complications.

III. THE PNEUMONIAS

A. Lobar Pneumonia

Lobar pneumonia is an acute infectious disease, caused by the pneumococcus, that is characterized by a severe toxemia and a massive exudate involving one or more lobes of the lungs.

Pathology.—The characteristic feature of lobar pneumonia is a massive inflammation of one or more lobes of the lungs with the formation of an exudate in the alveoli, bronchioles, and bronchi of the affected part.

The typical inflammatory reaction in the lungs passes successively through four stages which show considerable overlapping. These stages are: (1) engorgement, (2) red hepatization, (3) gray hepatization, and (4) resolution. In the stage of *engorgement* the lung is soft, flabby, and bright red in color. The alveoli contain an exudate of serum, red blood cells, and a small amount of fibrin. This stage lasts from a few to seventy-two hours. The exudate continues to pour into the alveoli and brings about the stage of *red hepatization* in which the affected portion of the lung is more or less solid, dark red in color, and covered with fibrin. The exudate in the alveoli coagulates. At this time the exudate also contains leucocytes and the causative organism. This stage lasts one or two days. When the body begins to overcome the pneumonic process, the red blood cells of the exudate are dissolved, but the other components are not affected which gives the lung a dirty gray appearance. This is the stage of *gray hepatization*. In the stage of *resolution* the exudate undergoes liquefaction and is removed partly by absorption and partly by expectoration, air enters the affected alveoli, the epithelium is replaced, and the lung returns to its former efficiency. As a rule resolution is complete within a week or ten days after the crisis, but in some cases it may not be complete for two or three months (delayed resolution). The plugging of the alveoli reduces the amount of oxygen in the blood (anoxemia) which leads to rapid, shallow breathing, increased pulse rate, nausea, vomiting, and cyanosis.

The blood usually shows an increase in leucocytes (30,000 to 40,000 per c.mm.) of which from 90 to 95 per cent are polymorphonuclear leucocytes. If such an increase does not occur, the prognosis is grave.

Complications.—Pleurisy is so often associated with lobar pneumonia that it is probably more logical to consider it a

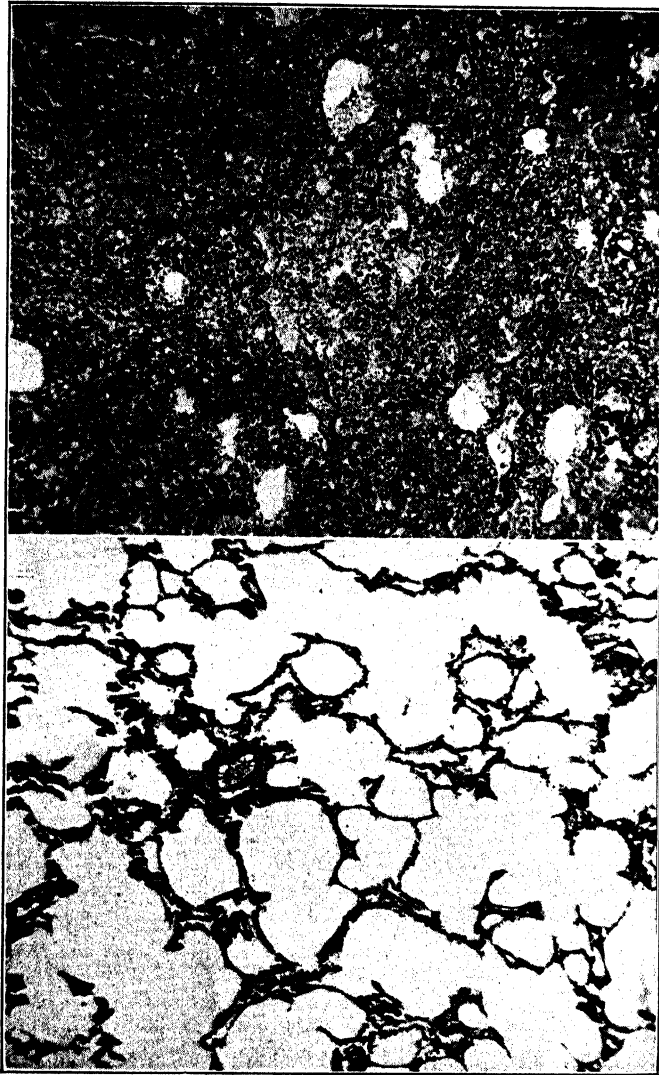


Fig. 128.—Sections showing the difference in a normal lung and one that is the site of a pneumonia. The section on the left shows normal lung tissue with open air spaces separated by thin walls. The one on the right shows a pneumonia. Note the air spaces filled with exudate.

part of the disease than a complication. Heart failure may occur, but is not as common as the general impression indicates. It is due to the action of toxins on the heart muscle and to the extra burden thrown on the right ventricle by the increase in resistance to the flow of blood through the lungs. Delayed resolution leads to a low grade fever and general malaise.

B. Bronchopneumonia

Unlike lobar pneumonia, *bronchopneumonia* is more often secondary than primary, may be due to any one of a number of organisms and, instead of being confined to one or more lobes, the pneumonic process consists of multiple small foci scattered throughout both lungs. It occurs most often in the early and late years of life.

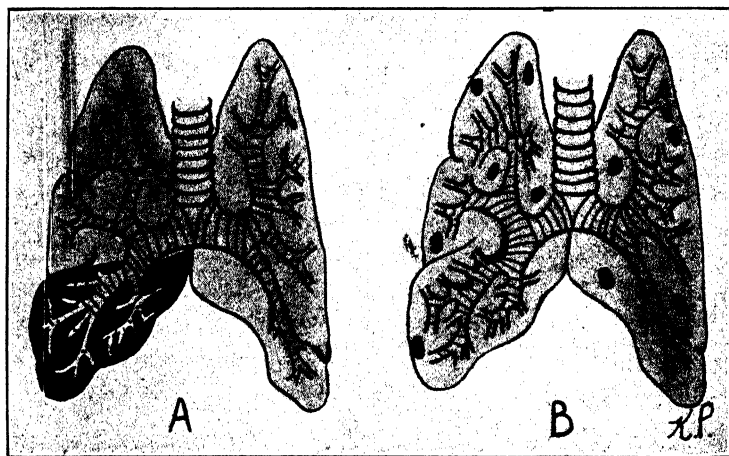


Fig. 129.—Diagrammatic illustration of distribution of (A) lobar and (B) bronchopneumonia. Pneumonic areas are represented by solid black.

Etiology.—Bronchopneumonia may be due to a variety of organisms, most important of which are streptococci, pneumococci, staphylococci, and *H. influenzae*. Important among the diseases that may be complicated, or followed, by bronchopneumonia are measles, influenza, whooping cough, and chronic diseases of the heart, blood vessels,

lungs, or kidneys. It may follow the taking of an anesthetic or the aspiration of infectious material into the lungs during operations. Bronchopneumonia of the newborn is often due to the aspiration of the contents of the birth canal. *Hypostatic pneumonia* is a bronchopneumonia following hypostatic congestion.

Pathology.—In bronchopneumonia patchy areas of inflammation are usually scattered throughout the lungs but are more numerous at the base. The involved alveoli contain leucocytes, epithelial cells, and bacteria but no fibrin or red blood cells. The number of leucocytes rises to from 20,000 to 40,000 per c.mm., and the causative organism is often found in the blood stream.

Complications.—Pleurisy and empyema are the most common complications.

IV. EPIDEMIC MENINGITIS

Pathology.—The essential pathology of epidemic meningitis is a localization of the meningococci in the nasopharynx with subsequent invasion of the blood stream, followed by localization in the meninges. About one-third of meningococcus infections are septicemias without localization in the meninges. When meningeal invasion occurs, an exudate composed of leucocytes, fibrin, meningococci, and red blood cells forms between the arachnoid and pia mater. The exudate is most prominent at the base of the brain, but it extends down the cord and into the ventricles. During this stage the cerebrospinal fluid may be so purulent that it will scarcely run through the spinal puncture needle.

The blood shows a distinct leucocytosis (15,000 to 60,000 per c.mm.; polymorphonuclears 85 to 90 per cent).

Complications.—Among the complications of epidemic meningitis are arthritis, hydrocephalus, otitis media, retinitis, deafness due to involvement of the eighth nerve, pericarditis, endocarditis, conjunctivitis, pneumonia, and blindness.

V. DISEASES CAUSED BY THE COLON-TYPHOID GROUP OF BACTERIA

A. Typhoid Fever

Typhoid fever is an acute infectious disease caused by *E. typhosa*. Pathologically it is characterized by swelling of the lymphoid tissue of the body, especially Peyer's patches, splenic enlargement, and bacteriemia. Clinically it is characterized by a continuous fever, a characteristic eruption, and a profound toxemia.

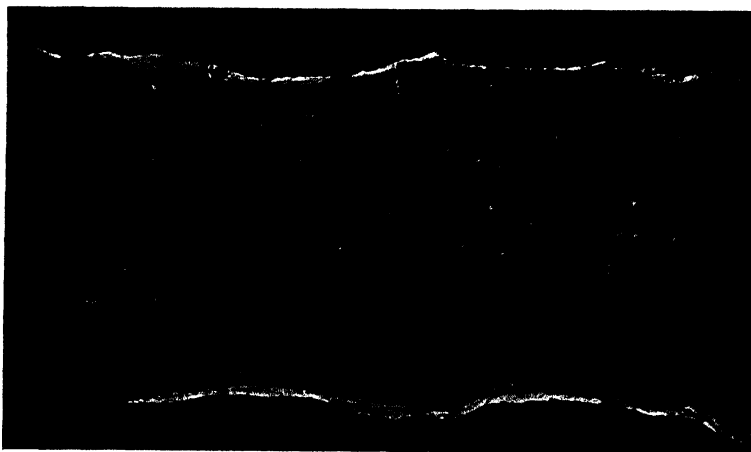


Fig. 180.—Ulceration of the intestine caused by typhoid fever. The ulcers extend in the direction of the long axis of the intestine. (From Mallory: *Principles of Pathologic Histology*. W. B. Saunders Co.)

Pathology.—Peyer's patches are the most important structures involved in typhoid fever. When they are attacked, they become swollen and project above the level of the intestinal mucosa in a plateau-like manner. In some cases necrosis and sloughing take place which leaves an oval ulcer of varying depth. If a blood vessel undergoes necrosis hemorrhage may occur, and if the ulcer extends deep enough perforation of the intestinal wall occurs.

The mesenteric lymph nodes are swollen and may suppurate. The spleen is soft and enlarged to two or three times its normal size. The liver often shows degenerative

changes, and the gallbladder may be inflamed. In some cases there is a degeneration of the myocardium. The kidneys may show cloudy swelling or other degenerative changes.

Except in the early days a leucopenia is always present in uncomplicated cases of typhoid fever. This may be due to the fact that typhoid bacilli have a selective action on the bone marrow. A leucocytosis in the latter days of the disease should lead to a strong suspicion of some complication.



Fig. 131.—Perforated typhoid ulcer of intestine. (From Karsner: *Human Pathology*. J. B. Lippincott Co.)

Complications.—Fully three-fourths of the deaths in typhoid fever are due to some complication. *Hemorrhage* occurs in about 7 per cent of cases, most often during the third week. As a rule pain does not occur and the passing of a tarry stool or clotted blood may be the first indication of hemorrhage. In severe hemorrhages the patient experiences a chill, the temperature drops, the pulse becomes rapid, and a leucocytosis develops. The mortality is about 25 per cent.

Perforation occurs in about 3 per cent of cases. The perforation is usually single but may be multiple and occurs

most often in the lower eighteen inches of the small intestine. The immediate cause of perforation may be increased peristalsis, accumulation of gas, straining at stool, unusual exertion, or the irritating effect of hard pieces of food. Perforation is usually accompanied by acute pain and is followed by peritonitis. The mortality is very high.

Cholecystitis occurs in about 2 per cent of cases. Typhoid bacilli may remain in the gallbladder for years after an attack of typhoid fever.

B. Bacillary Dysentery

Bacillary or epidemic dysentery is an infection due to *B. dysenteriae* which is characterized by a diffuse inflammation and ulceration of the large intestine, and sometimes the lower portion of the small intestine, which gives rise to abdominal pain, diarrhea, and constitutional symptoms. It affects adults between twenty and thirty years of age and children under two.

Pathology.—Early in the disease the mucous membrane of the colon becomes inflamed and undergoes necrosis which gives rise to shallow ulcers or, less often, extensive raw surfaces. The inflammation spreads until the entire large intestine and in some cases the last twelve to twenty-four inches of the small intestine are involved. In mild cases healing is complete, but severe cases may lead to extensive scarring of the intestine.

Complications.—Complications are not very common. The most common one is arthritis. In chronic dysentery profound anemia may be present and stenosis of the colon may be a sequel to severe cases.

VI. DISEASES CAUSED BY ACID-FAST BACILLI

A. Tuberculosis

Tuberculosis is an infectious disease caused by *Myco. tuberculosis* which attacks almost every tissue and organ of the body and brings about a variety of changes which depend to some extent on the tissue or organ attacked.

The term "tuberculosis" is derived from the small gray, white or yellow nodules (*tubercles*) that form a characteristic feature of the tissue changes brought about by *Myco. tuberculosis*. The parts of the body most often attacked are the lungs, intestines, and kidneys in adults, and the lymph nodes, bones, joints, and meninges in children.



Fig. 132.—Miliary tuberculosis of spleen. The white areas are miliary tubercles. (From Anderson: Synopsis of Pathology, The C. V. Mosby Co.)

Spread of *Myco. Tuberculosis* Within the Body.—Tubercle bacilli may be spread to different parts of the body by (1) the lymph stream, (2) the blood stream, (3) permeation of adjacent tissues, (4) the natural passages (example—from the kidneys to the bladder via the ureters), and (5) expansion over a surface. Of these methods, spread by the lymph stream is most common. Occasionally material heavily laden with tubercle bacilli (example—the liquefied center of a tubercle) breaks into a blood vessel and spreads widely over the body, forming many secondary foci. This is known as *miliary tuberculosis*. At other times the anatomy of the

affected vessel is such that a single organ is involved. If the tuberculous material breaks into the pulmonary artery one or both lungs will be affected; if into the portal vein, miliary tuberculosis of the liver will result, etc. This is known as *localized* miliary tuberculosis. The term "miliary" is used because the small tubercles found in this type of infection resemble millet seed.



Fig. 133.—Two miliary tubercles in an intestinal ulcer. Note attempted regeneration of surface epithelium. (From Karsner: *Human Pathology*, J. B. Lippincott.)

Pathology.—When tubercle bacilli first enter the body and attempt to produce disease, the body does not try to destroy them primarily by antibody formation and phagocytosis as it does many other bacteria, but there is a multiplication of tissue cells which has for its purpose the destruction of the bacilli by engulfing them or forming restricting barriers around them. This leads to the formation of firm, round or oval, white, gray or yellow nodules from 1 mm. to 3 cm. in diameter, known as *tubercles*. A tubercle consists of an inner zone containing tubercle bacilli, epithelioid cells, and giant cells surrounded by a middle zone of lymphoid cells,

and an outer zone of fibrous tissue. Their microscopic appearance is so characteristic as to be diagnostic even though no tubercle bacilli are found. A tubercle may enlarge singly or a number of small tubercles may coalesce to form a large tubercle, known as a conglomerate tubercle. On account of the accumulation of cells and proliferation of fibrous tissue at the periphery of the tubercle the blood vessels are compressed and the nutrition of the tubercle is interfered with. This leads to a peculiar type of necrosis of the center of the tubercle that is characterized by the presence of a large amount of greasy lipid material. This is known as *caseation necrosis*.

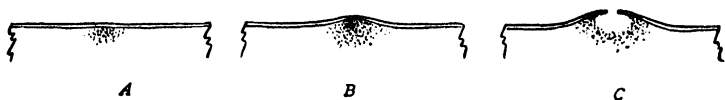


Fig. 134.—Diagrammatic illustration of the formation of a tuberculous abscess or ulcer. (From Pottenger: *Clinical Tuberculosis*. The C. V. Mosby Co.)

The caseous tubercle may remain unchanged for a long time or it may become walled off with connective tissue, undergo calcification, become organized, or undergo liquefaction. Calcification is a reparative process, brought about by the deposit of lime salts in the necrotic tissue. In organization the necrotic material is at least partially removed and replaced by connective tissue. In certain parts of the body liquefaction leads to the formation of cold abscesses; in the lungs it may convert a closed tuberculosis into an open one, and it may convert tubercles situated near the surface of the body into ulcers. Let it be remembered that regardless of the reparative processes that a tubercle has undergone, it may still contain living tubercle bacilli.

Pulmonary Tuberculosis.—Pulmonary tuberculosis is the most common type of the disease and is due to the human bacillus. It is infrequent in children but when it does occur, it is rapidly fatal.

Pulmonary tuberculosis may occur in the form of conglomerate tubercles of the apex, miliary tuberculosis, or pneumonic tuberculosis. Conglomerate tubercles of the apex



Fig. 135.—Tuberculosis of the lungs. A large cavity is seen in the upper lobe. The lower lobe shows several tuberculous nodules and small cavities. (Beattie and Dickson.) (From Woolley: *Fundamentals of Pathology*. The C. V. Mosby Co.)

(apical tuberculosis) is by far the most common type, and its site is most often the right apex. After a conglomerate tubercle of the apex has been established, it becomes surrounded by a fibrous capsule in cases that progress favorably. The center of the tubercle may remain caseous, undergo calcification, or become converted into a fibrous mass by an overgrowth of connective tissue from the capsule. In unfavorable cases the tubercle continues to grow with little capsule formation, and in cases that have been progressing favorably but have taken an unfavorable turn, the capsule that has already formed undergoes caseation necrosis. The center of the tubercle undergoes liquefaction, and the cavity thus formed continues to enlarge and finally opens into a



Fig. 136.—Tuberculous ulcers of intestine. The ulcers extend in a direction transverse to the long axis. (Delafield and Prudden.) (From Woolley: *Fundamentals of Pathology*.)

bronchus. After a communication has been established between the cavity and a bronchus, the cavity continues to enlarge, secondary infection becomes more extensive, hemorrhage may occur, and the amount of expectorated material increases. Hemorrhage is due to the erosion of a blood vessel wall to such an extent that rupture takes place. Secondary infection is most often due to streptococci or staphylococci and is frequently responsible for the hectic fever that often occurs in tuberculosis.

A tuberculous cavity may not be more than one or two centimeters in diameter, or it may involve a whole lobe of the lung. Obliterated bronchi and blood vessels may extend through the cavity. In some cases bands of connective tissue arise from the neighborhood of the capsule and extend

through the pulmonary tissue. Contraction of the bands causes great shrinking of the affected lung. This is known as *fibroid phthisis*.

Miliary tuberculosis of the lungs occurs most often as a part of a generalized miliary tuberculosis but may occur as a local process when a tuberculous focus opens into the pulmonary artery.

A very acute pulmonary tuberculosis may take the form of a lobar or bronchopneumonia. This form of the disease often kills within a few days.

Tuberculous Pleurisy.—Tuberculous pleurisy is most often secondary to tuberculosis of the lungs. Pleural effusion (collection of liquid in the pleural cavity) often accompanies it, and all pleural effusions should be considered of tuberculous origin until proved otherwise.

Tuberculosis of the Intestines.—Tuberculosis of the intestines occurs most often in adults and is usually secondary to pulmonary tuberculosis. In children it is usually a primary infection due to the ingestion of unpasteurized milk from tuberculous cows. Intestinal tuberculosis most often affects the lower end of the ileum and the cecum. In the beginning tubercles form in the subepithelial lymphoid follicles and in Peyer's patches. The overlying epithelium breaks down, forming ulcers that tend to encircle the intestine. Perforation is not common, but the peritoneal surfaces of the ulcers often become adherent to adjacent structures. Contraction of the scars formed by the healing of ulcers may lead to obstruction of the intestine.

A hyperplastic form of tuberculosis, in which there is little tubercle formation and caseation but a marked increase in submucosal connective tissue, often affects the cecum and may involve the appendix. The cecum becomes enlarged and firm, and the mass may be mistaken for a tumor.

B. Leprosy

Leprosy is a chronic infectious disease which is characterized by a variety of lesions that involve the skin and other parts of the body and lead to extensive deformity and destruction of tissue.

Pathology.—From the pathological standpoint leprosy belongs with the infectious granulomas; i.e., diseases in which a defensive multiplication of tissue cells, instead of an ordinary inflammatory reaction, occurs at the site of infection.

Although leprosy is a general disease, certain local lesions are conspicuous and serve to establish the two important forms of the disease, the nodular and the anesthetic. The first is characterized by a tumorlike overgrowth of the skin. The latter is characterized by the presence of localized areas of skin anesthesia.

VII. DISEASES CAUSED BY BACTERIA PRODUCING EXTRACELLULAR TOXINS

A. Diphtheria

Diphtheria is an acute infectious disease due to *C. diphtheriae*. It is characterized by systemic disturbances and the formation of a pseudomembrane at the site of infection. The systemic disturbances and organic changes characteristic of the disease are due to an extracellular toxin. The most common sites of infection are the tonsils, pharynx, larynx, and nasal passages. Much less often diphtheria attacks the vulva, conjunctiva, skin, or wounds.

Pathology.—The local lesions of diphtheria are remarkably alike, regardless of location. At first there is a degeneration of the surface cells of the affected area. This is followed by an abundant fibrinous exudate that leads to the formation of a thick, tough pseudomembrane which has a remarkable tendency to spread. When the pseudomembrane is pulled off, a bleeding surface is left, but a new pseudomembrane soon forms. The pseudomembrane is composed of fibrin, leucocytes, red blood cells, bacteria, and dead epithelial cells. In ordinary pharyngeal diphtheria the pseudomembrane begins on one or both tonsils and spreads to the uvula and soft palate. In nonfatal cases not receiving antitoxin the pseudomembrane persists for a week or ten days and then disappears. It may obstruct breathing or even produce suffocation. It should be remembered that organisms other than *C. diphtheriae* may produce pseudomem-

branes, and in a few cases of diphtheria pseudomembrane formation does not occur.

The action of diphtheria toxin on the heart causes fatty degeneration and myocarditis which often leads to heart failure. Cardiac failure usually occurs after the other manifestations of the disease have begun to subside, and it may occur in comparatively mild cases. For this reason it is imperative that patients with diphtheria be kept in bed long after the acute manifestations of the disease have subsided. Degeneration of the peripheral nerves brought about by the toxin may lead to late paralysis, particularly of the palate. The toxin may produce nephritis and necrosis of the liver.

Complications.—With the exception of cardiac failure and paralysis, bronchopneumonia is the most important complication.

B. Tetanus

Pathology.—The pathological changes brought about by tetanus (lockjaw) are due to the action of the toxin of *Cl. tetani* on the central nervous system. Even after death occurs there are few gross changes in the body, and the spinal fluid is normal. The spasms originate in the central nervous system, and the impulses are transferred to the muscles by the motor nerves.

VIII. DISEASES CAUSED BY SPIROCHETES

Syphilis*

Primary Stage.—A chancre usually appears beneath the mucous membrane or skin as a small nodule having the feel of a shot. It then breaks down forming a shallow ulcer with indurated edges. There is little pain or discharge unless a secondary infection occurs. Chancres are usually single but may be multiple. They vary in size but are seldom more than one-half inch in diameter. A few days after the chancre appears, the lymph nodes draining its site become enlarged.

*Before reading the pathology of syphilis the student should carefully review its microbiology (page 392).

Pain is absent and the nodes show no tendency to suppurate. In the female the chancre is often situated on the cervix. In the male it frequently occurs within the urethra. In untreated cases the chancre heals in about four or five weeks. Chancres contain many treponemas but the treponemas have already spread to all parts of the body before the chancre makes its appearance.



Fig. 137.—Two gummas of the liver. (From Boyd, William: *Surgical Pathology*. W. B. Saunders Co.)

Secondary Stage.—The characteristic pathological features of the secondary stage of syphilis are (1) skin lesions, (2) lesions of the mucous membranes, and (3) general lymphadenopathy. The skin lesions consist of a typical eruption, loss of eyebrows, and a patchy loss of hair. The skin eruption is usually symmetrically arranged, macular and copper colored. It seldom itches or burns. The lesions of the mucous membrane are known as *mucous patches*. They are painful superficial ulcers with a white raised surface and are literally swarming with treponemas. Mucous patches are found most often in the mouth.

Tertiary Stage.—The most characteristic lesion of tertiary syphilis is the *gumma* which consists of a firm, yellowish white central portion surrounded by fibrous tissue. The

tertiary lesions most often involve the deeper structures of the body and may interfere with the activities of the internal organs.

Syphilis seems to have a predilection for the heart and vascular system. It is responsible for certain aneurysms and valvular diseases of the heart and probably predisposes to arteriosclerosis. Other organs and systems frequently attacked by syphilis are the respiratory system, bones, joints, reproductive organs, and nervous system.



Fig. 138.—Hutchinson's teeth. (From Mead: *Diseases of the Mouth*. The C. V. Mosby Co.)

Prenatal Syphilis.—The term prenatal syphilis refers to the disease acquired before birth. It is often spoken of as congenital or hereditary syphilis. The latter is a bad term which indicates that the disease is transferred from parent to offspring in accordance with the laws of heredity. For prenatal syphilis to occur, the mother must be infected. The treponema pass by way of the blood stream to the maternal side of the placenta and are deposited. Syphilitic foci develop in the placenta and the organisms spread through the fetal circulation to the fetus.

The manifestations of congenital syphilis may be classified as early and late. The early manifestations usually appear a few weeks after birth or are present at birth. The

child of a syphilitic mother may (1) be born dead, (2) be born alive with evidence of syphilis, (3) be born apparently in good health but show evidence of syphilis after it is several weeks or months old, or (4) entirely escape the disease. Infants born with evidence of active syphilis are undersized and have an appearance strikingly like that of an old man. A vesicular skin eruption and a persistent discharge from the nose (snuffles) are often present, and the child may have linear scars at the angles of the mouth (syphilitic rhagades). Among the later manifestations of congenital syphilis are poorly developed, small peg-shaped permanent teeth. The upper central incisors are often wedge-shaped and show a central notch (Hutchinson's teeth). Other late manifestations of congenital syphilis are interstitial keratitis, anterior bowing of the tibia (sabre tibia), dactylitis, and neurosyphilis. The placenta of a syphilitic child is often relatively large for the weight of the child.

Neurosyphilis.—When syphilis is becoming generalized during its early stages the central nervous system seldom escapes invasion. In many cases the treponemas die without causing any changes in the central nervous system, but in from 30 to 40 per cent of cases they remain alive and cause changes that become apparent weeks, months, or years later. Depending on the tissue primarily attacked neurosyphilis takes three characteristic forms: (1) syphilitic meningitis in which the meninges are primarily attacked, (2) tabes dorsalis in which there is a parenchymatous degeneration of certain portions of the spinal cord, and (3) general paresis in which there is a parenchymatous degeneration of the brain. In addition to these manifestations gummas may occur in various portions of the central nervous system.

The characteristic symptoms of early neurosyphilis, regardless of type, are headache, vertigo, blurring of vision, and optic neuritis.

Congenital neurosyphilis simulates the acquired form and may make its appearance in early life or may be delayed to adolescence or even later.

Neurosyphilis may simulate almost any disease of the central nervous system but a careful history with a correct

interpretation of laboratory tests on the blood and spinal fluid usually make their differentiation possible.

Cardiovascular Syphilis.—By cardiovascular syphilis is meant, from a practical standpoint, syphilis of the aorta and its complications (aortic insufficiency, aneurysm, etc.).

Syphilis of the Lungs.—In stillborn syphilitic children the lungs fill the entire thoracic cavity and are grayish white in color. The alveoli are incompletely developed or not developed at all. This condition is known as white pneumonia or *pneumonia alba*, and forms a pathognomonic sign of congenital syphilis.

IX. DISEASES CAUSED BY PROTOZOA

Malaria

The characteristics of the malaria parasite, mode of infection, and cause of symptoms in malaria were discussed in the section of this book devoted to Microbiology (see page 419).

Pathology.—The chief pathological changes brought about by malaria are destruction of red blood cells, thrombosis of the capillaries by the parasites, splenic enlargement and, less often, enlargement of the liver. The destruction of red blood cells leads to anemia and malarial hemoglobinuria. The white blood cells may increase during the paroxysm, but in the interim they are normal. A plugging of the capillaries similar to that occurring in the brain in the comatose form of pernicious malaria occurs in certain portions of the gastrointestinal tract in algid malaria. In acute malaria the spleen is moderately enlarged, soft, and friable. In chronic malaria it is enlarged and may be fibrosed to such an extent that it ruptures as the result of a blow or fall or even spontaneously. Malaria promotes laziness, retards mental activity, and lowers the economic status of the victim.

Questions for Review

1. Name some common complications of scarlet fever; of acute rheumatic fever.
2. Compare lobar and bronchopneumonia from the standpoint of cause and pulmonary changes.

3. What tissues are primarily attacked by the typhoid bacillus?
4. What is miliary tuberculosis?
5. What organs or tissues are most often attacked by tuberculosis in children? In adults?
6. How do tubercle bacilli spread over the body?
7. Name and describe the characteristic lesion of tuberculosis.
8. Why is it imperative that a patient with diphtheria be kept in bed until convalescence is complete?
9. Give some of the signs that will be observed when a child is born with active syphilis.
10. Name three forms of syphilis of the central nervous system and give the important characteristic of each.

True-False Test

Place the word "true" or "false" before each statement.

- 1. Both lobar and bronchopneumonia are usually brought about by several different organisms.
- 2. Bronchopneumonia attacks children, the aged, and persons in a debilitated condition more often than others.
- 3. A leucocytosis in typhoid fever is a sign of good omen.
- 4. A chill after the first week of typhoid fever, a sudden drop in temperature or a rise in pulse rate, points to a complication.
- 5. Miliary tuberculosis is a very mild form of the disease.
- 6. If the child of a syphilitic mother does not show signs of syphilis at birth, the child may be considered free of the disease.
- 7. Snuffles, rhagades and Hutchinson's teeth are all signs of prenatal syphilis.
- 8. Prenatal syphilis never attacks the central nervous system.
- 9. The gumma is the characteristic lesion of tertiary syphilis.
- 10. Malaria parasites attack the red blood cells.

Completion Test

1. The course of most infectious diseases falls into several different periods:
 1. -----
 2. -----
 3. -----
 4. -----
 5. -----
2. List the pathological changes that are found in nearly every infectious disease.
 1. -----
 2. -----
 3. -----

4. -----
5. -----
3. ----- and ----- are two complications to be dreaded in typhoid fever.
4. The primary lesion of tuberculosis is known as -----.
5. Tuberculosis of the intestines is most often secondary to tuberculosis of the -----.
6. Pleural effusions are often due to -----.
7. The characteristic lesions of the mucous membrane in secondary syphilis are known as ----- They are found most often in the ----- and are highly infectious.
8. A syphilitic child is often ----- than normal and the placenta is often comparatively ----- for the size of the child.

References

- Osler, William: Principles and Practice of Medicine, New York, 1947, D. Appleton-Century Co.
- Anderson, W. A. D.: Synopsis of Pathology, St. Louis, 1946, The C. V. Mosby Company.
- Strong, Richard P.: Stitt's Diagnosis, Prevention and Treatment of Tropical Diseases, Philadelphia, 1942, P. Blakiston's Son and Co.
- Zahorsky and Zahorsky: Synopsis of Pediatrics, St. Louis, 1948, The C. V. Mosby Co.
- Meakins, J. C.: The Practice of Medicine, St. Louis, 1944, The C. V. Mosby Co.
- Boyd, William: A Textbook of Pathology, Philadelphia, 1947, Lea & Febiger.

CHAPTER XLV

THE VITAMIN DEFICIENCIES

I. GENERAL CHARACTERISTICS OF VITAMINS

That certain food principles other than proteins, carbohydrates, fats, and inorganic salts were necessary for the growth, development, and continued well-being of the body was not recognized until the early part of the present century. These substances, whose mode of action is yet not well understood, are known as *vitamins* or *food accessory factors*. With but one exception they manifest themselves by their absence instead of their presence or overabundance; i.e., symptoms occur only when the body is deficient in vitamins. When there is a deficiency in certain vitamins the nutrition of the body as a whole suffers, and in addition a train of symptoms characteristic of a deficiency in that particular vitamin occurs. Such diseases are known as *vitamin deficiency diseases* or *avitaminoses*. A deficiency in more than one vitamin is sometimes spoken of as *polyavitaminosis*. There are deficiencies other than vitamin deficiencies. Among these are deficiencies of calcium, iodine, or iron.

The vitamins are identified by the letters of the alphabet, but the letters used have no relation to the order of their discovery. The term vitamin, which means "life amin," is not well used because it indicates that the vitamins are amins and that they are all chemically related, neither of which is true. However, they do have several common characteristics, among which are the following: (1) all are necessary for the absorption of food and maintenance of growth and health; (2) each has its own specific action; (3) their presence in very small amounts is sufficient to meet the needs of the body; (4) they are products of the vegetable kingdom and cannot be produced by the animal body;* (5) their ac-

*Although animal tissues and fluids are often the source of vitamins, the vitamins originally came from the plant world.

tion is somewhat like that of enzymes; and (6) a given vitamin may be abundantly present in one food and absent from another.

More than a dozen vitamins have been identified and studied. The following is an outline of the most important of these:

1. **Vitamin A (Antixerophthalmic, Anti-infection).**—Vitamin A is found in butter, codfish, egg yolk, carrots, sweet potatoes, squash, animal fats, and green-leaved vegetables. In the animal body it is manufactured by the liver from the carotene of vegetable foods. It is necessary for the proper development of the young, and when it is deficient, a peculiar type of ophthalmia (xerophthalmia) develops and night blindness occurs. The surface epithelium becomes keratinized and that of the respiratory system and intestines becomes transformed into stratified squamous epithelium. All of this increases susceptibility to infections. Tooth changes occur. This vitamin is fat-soluble.

2. **Vitamin B Complex.**—The vitamin B complex, found in wheat germ, rice polishings, and yeasts, was once thought to be a single vitamin and was known as vitamin B. Subsequently, it has been separated into two parts (B_1 and B_2) and has been found to consist of at least six vitamins. Vitamin B_1 is known as the *antineuritic factor* and its active principle is *thiamine hydrochloride*. It prevents beriberi. Vitamin B_2 (also known as vitamin G) is composed of *nicotinic acid*, which has a preventive and curative effect on pellagra in man and black tongue in dogs, and *riboflavin*, which seems to be necessary for growth. A recently synthesized member of the vitamin B complex is folic acid, which is assuming a place of importance in the treatment of sprue and various types of anemia.

3. **Vitamin C (Antiscorbutic).**—Vitamin C has been identified as *ascorbic acid*. It is found in germinating grains and the juices of fruits, especially orange and lemon juices. Its deficiency leads to dental decay and scurvy.

4. **Vitamin D.**—Vitamin D has been called the *sunray* or *antirachitic* vitamin. It is a component of codfish, butter, yeast, and egg yolk. Ergosterol, which was formerly ob-

tained from ergot but is now obtained from yeasts and other substances, when exposed to ultraviolet light, develops a vitamin D potency greater than that of cod-liver oil. Such irradiated ergosterol is known as *viosterol*. Sunlight or artificial ultraviolet light increases the vitamin D content of the body by converting the ergosterol of the skin and tissues into vitamin D. According to some workers the substance in the skin that is converted into vitamin D is not ergosterol but eleidin, a closely related compound. A deficiency in vitamin D leads to tooth decay and rickets. So far as is known this is the only vitamin whose overabundance leads to bad effects. It leads to abnormal porousness of the bones and the deposit of calcium in the soft tissues.

5. **Vitamin K.**—Vitamin K, which is necessary for the formation of prothrombin (an essential element in blood coagulation), is ingested in the form of certain green foods or is formed in the intestinal canal by the action of intestinal bacteria on the intestinal contents. Certain hemorrhagic states in the newborn infant and the hemorrhagic tendencies in certain cases of jaundice may be explained on the basis of a reduction in, or absence of, vitamin K. In the case of the newborn infant the prothrombin received from the mother's circulation is used before sufficient vitamin K to furnish enough prothrombin for blood coagulation is ingested in the food or is formed by the intestinal bacteria. In case of jaundice of the obstructive type vitamin K may not be absorbed from the intestinal canal because of the absence of bile which is essential for the absorption of vitamin K.

II. RICKETS (RACHITIS)

Rickets is a constitutional disease of infancy that is due, at least in part, to a diet that is deficient in vitamin D. It is fundamentally an overproduction of osteoid tissue that is deficient in calcium and phosphorus. The disease probably occurs most often in those who possess an inherited predisposition to it. The outstanding clinical feature of rickets is marked by bone deformity, especially affecting the long bones and the bones of the skull.

Rickets is primarily a disease of the city. It is more common in Negroes than in white people. Breast-fed children do

not develop it as often as the artificially fed. The disease seldom begins during the summer months, and developed cases usually improve at this time of the year. This is because sunlight is abundant in the summer and its ultraviolet rays protect against rickets by producing vitamin D from the ergosterol (or eleidin) contained in the superficial layers of the skin. For the same reason children who live where there is an abundance of sunlight are not as likely to develop



Fig. 139.—Child with rickets. (From Woolley: Fundamentals of Pathology.)

rickets as those who live in dark surroundings. Window glass removes the ultraviolet rays from sunlight, and the pigment of the skin protects ergosterol against their action. For this reason children who live indoors are more likely to develop rickets than those who live outdoors, and Negroes are more likely to develop it than whites.

Rickets usually begins between the sixth and eighteenth month of life and remains active for one or two years and

then subsides, but the deformities produced by the disease may remain throughout life.

Since the bones are deficient in lime salts they are soft and as the disease progresses they suffer greater and greater deformity. The ankles and wrists are greatly thickened and the bones may be cut with a knife. Dentition is delayed and the teeth are defective. The flat bones of the skull are thin and the fontanels close slowly. A peculiar enlargement of the junctions between the ribs and sternum, known as "*the rachitic rosary*," is a characteristic sign of rickets. Pigeon chest, bowlegs and knock-knees are common deformities. Advanced cases show flattening of the pelvis and marked deformity of the spine. The rachitic child is often pot-bellied and has a large square head but as a rule appears well nourished or even obese. Diffuse soreness of the body, nocturnal restlessness, slight fever, and profuse sweating of the head and neck are common symptoms. Complications of an infectious nature are not uncommon.

III. PELLAGRA

Pellagra is a rather common deficiency disease that is characterized by a seasonal variation, a tendency to recur, and a rather characteristic train of symptoms consisting of a skin eruption, gastrointestinal disturbances, and nervous and mental changes.

It was once thought that pellagra was due to a diet containing spoiled maize. At a later period it was thought to be of infectious origin and many theories concerning its causative organism and mode of transmission were proposed. At the present time it is thought that the primary factor in the production of pellagra is a diet that is deficient in nicotinic acid, but it is also conceded by many that some other condition is a secondary factor. Depleting diseases and the prolonged use of alcohol seem to be predisposing influences.

Pellagra often begins in the spring and recurrences are more common at that time. The characteristic manifestations of the disease are frequently preceded by such prodromal signs as loss of appetite, digestive disturbances, mental depression, etc. The eruption usually begins on the exposed

surfaces of the body and is often mistaken for sunburn, which it closely resembles at first. After persisting from a few days to several weeks the eruption terminates by desquamation or vesicle or bullae formation. The tongue and mouth are red, raw, swollen, and ulcerated. A distressing salivation may be present. The intestines are often ulcerated. Hydrochloric acid is frequently absent from the stomach and a severe diarrhea occurs in about three-fourths of the patients. There is



Fig. 140.—Eruption on hands of patient with pellagra. (From Ruffin and Smith: *South. M. J.* 32: 40, 1939.)

an atrophy of various organs and tissues, and the patient may undergo a degree of emaciation seldom seen in any other disease. The central nervous system shows microscopic but no gross changes, and 40 per cent of the patients suffer mild or severe mental disturbances. When the triad of skin eruption, gastrointestinal disturbance, and mental symptoms is present, the diagnosis of pellagra is easy, but one or more are often absent.

The prognosis is uncertain but it is much worse in acute than in chronic cases, and in chronic cases the prognosis in each exacerbation is worse than in the one before. Mild cases often become severe, and from 5 to 10 per cent of patients with pellagra become permanently insane. Fever or mental symptoms give the disease a bad outlook and the outlook is worse in the aged than in the young. In spite of the uncertainty of the outcome in a given case the mortality in pellagra is less than 10 per cent.

IV. BERIBERI

Beriberi is a multiple neuritis due to a diet deficient in vitamin B₁ (thiamine hydrochloride) that is characterized clinically by disturbances in sensation and motion, dropsy, and involvement of the heart. It is seen most often in countries where the diet consists chiefly of highly milled rice, but it may occur in persons whose diet consists mostly of highly milled grains other than rice or in those who subsist on canned foods. That beriberi occurs in those whose diet consists chiefly of highly polished grains while it does not occur in those whose diet consists chiefly of the same grains that have not been highly milled is because in the latter the outer layers of the grain, which contain sufficient vitamin B₁ to prevent the disease, have not been removed.

Beriberi occurs in two forms: *wet*, characterized by general edema, and *dry*, characterized by various muscular palsies. A few cases are characterized by an early and serious involvement of the heart which may cause sudden death. The symptoms of the disease are such that it may be mistaken for nephritis or locomotor ataxia. Atrophy, degeneration of the nerves, enlargement of the right side of the heart, anasarca, and effusions in various cavities are found at autopsy.

While the course of a given case is uncertain and cardiac involvement may lead to sudden death, complete recovery is frequent. The mortality ranges from 3 to 5 per cent.

V. SCURVY

Scurvy is a deficiency disease due to a lack of vitamin C (ascorbic acid), which is usually brought about by an ex-

clusion of fresh food from the diet. Until a few decades ago scurvy broke out among the sailors on every long sea voyage, and in war more soldiers died from scurvy than from wounds. Since the antiscorbutic action of fresh foods, especially lemons and oranges, has become generally understood, scurvy has become a much less important disease than it was in the past.

Scurvy begins with weakness, anemia, and general signs of ill health, which are followed by sponginess, swelling, and bleeding of the gums, with capillary hemorrhages in other parts of the body, particularly from the nose and kidneys. The breath becomes very foul; the teeth loosen and fall out, and the legs become swollen and so painful that the patient is rendered helpless.

Infantile scurvy (Barlow's disease) usually affects children between 6 and 12 months of age. The child does not progress satisfactorily and the appetite is poor. This is the most common form of scurvy. If scurvy has progressed extensively the heart may show signs of damage after the other signs of the disease have subsided. Patients with scurvy are very susceptible to secondary infections, especially pneumonia.

True-False Test

Place the word "true" or "false" before each statement.

- 1. Vitamin A deficiency results in a susceptibility to infections.
- 2. Night blindness is a result of vitamin B deficiency.
- 3. The active principle of vitamin B₂ is thiamine hydrochloride.
- 4. Nicotinic acid is given to prevent pellagra.
- 5. Overabundance of vitamin D leads to abnormal porousness of the bones and the deposit of calcium in the soft tissues.
- 6. Vitamin K is absorbed from the intestines only in the presence of bile.
- 7. Vitamin C is produced by the action of intestinal bacteria.
- 8. Hemorrhage frequently occurs with obstructive jaundice.
- 9. Deformities produced by rickets may remain throughout life.
- 10. Rickets result from an overproduction of osteoid tissue that is deficient in calcium and phosphorus.
- 11. Rickets is primarily a disease of the city.

Completion Test

1. A peculiar enlargement of the junction between the ribs and sternum known as "-----" is a characteristic sign of rickets.
2. Three symptoms characteristic of pellagra are:
 1. -----
 2. -----
 3. -----
3. ----- is frequently absent from the stomach of pellagra patients.
4. Beriberi is a multiple neuritis due to a diet deficient in vitamin -----.
5. Scurvy is a deficiency disease due to the lack of vitamin -----.
6. List four symptoms of scurvy.
 1. -----
 2. -----
 3. -----
 4. -----
7. Patients with scurvy are very susceptible to -----.

References

- Bard, Philip, and Collaborators: *MacLeod's Physiology in Modern Medicine*, St. Louis, 1941, The C. V. Mosby Co.
- Wright, Samson: *Applied Physiology*, New York, 1945, Oxford University Press.
- Duncan, Garfield G.: *Diseases of Metabolism*, Philadelphia, 1947, W. B. Saunders Co.
- Anderson, W. A. D.: *Synopsis of Pathology*, St. Louis, 1946, The C. V. Mosby Co.
- Meakins, J. C.: *The Practice of Medicine*, St. Louis, 1944, The C. V. Mosby Co.
- Boyd, William: *A Textbook of Pathology*, Philadelphia, 1947, Lea & Febiger.

CHAPTER XLVI

DISTURBANCES IN SIZE, GROWTH, AND DEVELOPMENT OF CELLS AND TISSUES

The cells making up a part of the body may undergo changes in size, number, or type. These changes, acting singly or in combination with each other, may lead to atrophy, hypertrophy, hyperplasia, or metaplasia.

I. Atrophy

Atrophy is a decrease in the size of a part of the body brought about by a decrease in the size (simple atrophy) or number (numerical atrophy) of its cells. Simple atrophy is not as important as numerical atrophy because all extensive atrophies are brought about by a decrease in the number of cells, i.e., they are numerical atrophies. When an organ undergoes atrophy, its functioning tissue is primarily affected. Atrophy may be physiological or pathological. Physiological atrophy is best represented by the atrophy of the thymus gland in children, the atrophy of the mammary glands after lactation, and the more or less generalized atrophy of all organs and tissues that occurs in old age (senile atrophy).

The general causes of pathological atrophy are: (1) decrease in nourishment, (2) disuse, (3) pressure, (4) overwork, (5) nervous influences, and (6) influences exerted by the endocrine glands. When there is a serious interference with general nourishment over a considerable period of time, as occurs in starvation and wasting diseases, the body undergoes more or less generalized atrophic changes. Localized atrophy, as is sometimes seen in an extremity, is often caused by a restriction of nourishment resulting from an interference with blood supply. Atrophy from disuse is most often seen in the muscles of paralyzed limbs and muscles attached to immobilized joints. Pressure atrophy is best exemplified by the atrophy brought about by the pressure exerted by tumors and aneurysms. Bone is more susceptible to pressure atrophy than soft tissues. Atrophy from overwork is best exempli-

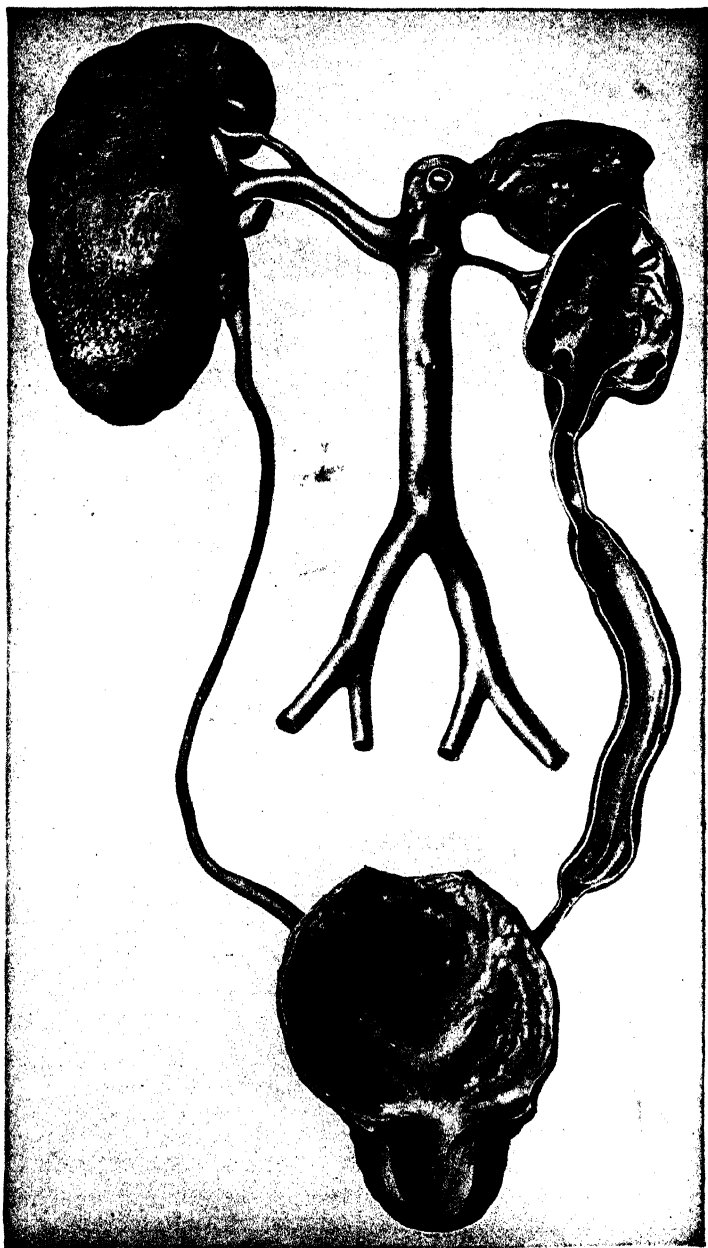


Fig. 141.—Atrophy of left kidney following obstruction of the ureter. The opposite kidney has undergone a compensatory hypertrophy. (From MacCallum: *A Textbook of Pathology*. W. B. Saunders Co.)

fied by the atrophy of the salivary glands in those who constantly chew tobacco or gum. Atrophy of the hair follicles and sebaceous glands in myxedema (caused by a deficiency in the activity of the thyroid gland) is an example of atrophy due to disturbance of the endocrine glands.

Atrophic organs are often irregular on the surface on account of the uneven distribution of the atrophic foci within them.

II. Hypertrophy

Hypertrophy is an increase in the amount of functioning tissue of an organ or part, caused by an increase in the functional demands made upon it. The enlargement may be due to an increase in the size of the cells (simple hypertrophy), an increase in the number of cells (numerical hypertrophy), or both. Most hypertrophies are of the last type, i.e., a combination of simple and numerical hypertrophy. Numerical hypertrophy should not be confused with hyperplasia. The latter does not arise in response to an increase in function.

Hypertrophy may be either physiological or pathological. Examples of physiological hypertrophy are the increase in size of the muscles as a result of exercise and the increase in size of the uterus and breasts during pregnancy. Pathological hypertrophy may be adaptive or compensatory. An example of an *adaptive hypertrophy* is the thickening of the walls of the urinary bladder resulting from a long-continued obstruction to the outflow of urine, or the hypertrophy of heart muscles in certain valvular lesions of the heart (see page 584). *Compensatory hypertrophy* is an enlargement of the remaining organ or tissue after a portion has been rendered inactive. For instance, if one kidney is removed, the other enlarges.

III. Hyperplasia

Hyperplasia is an increase in the number of cells of a part brought about by irritation of inflammation. The organ is enlarged but no increase in functional activity accompanies the enlargement. A good example of hyperplasia is the enlargement of the prostate that occurs in old age. Although this condition is often referred to as hypertrophy, it is in

reality a hyperplasia. It is often difficult to determine whether we are dealing with a hyperplasia or a malignant overgrowth; the former may be a forerunner of the latter, as is sometimes seen in the development of malignant tumors of the breast or prostate gland.

IV. Metaplasia

Metaplasia is the conversion of one type of tissue into another. It never oversteps the boundaries of the primary groups of tissue (epithelium, connective tissue, blood and lymph, muscle and nerve tissue), i.e., one type of epithelium may be converted into another type of epithelium but not into connective tissue, while one type of connective tissue may change into another type but not into epithelium. Examples of metaplasia are the conversion of the columnar epithelium of the gall bladder into the squamous variety in the presence of gallstones, and the conversion of the laryngeal and tracheal cartilage into bone in the aged. The causes of epithelial metaplasia are inflammation, extremely rapid growth, or vitamin deficiency. Connective tissue hyperplasia may be caused by chronic inflammation, necrosis, or the aging process. Metaplasia of tissues other than epithelium and connective tissue seldom if ever occurs.

Questions for Review

1. Classify and define the types of atrophy.
2. What are the general causes of pathological atrophy?
3. Give several examples of physiological hypertrophy.
4. Distinguish between hypertrophy and hyperplasia.
5. What are the causes of epithelial metaplasia?

True-False Test

Place the word "true" or "false" before the following statements:

- 1. The wrinkled skin seen in old people is an example of simple atrophy.
- 2. In numerical atrophy, there is a decrease in the number of cells of a part.
- 3. In old age there is a tendency for the entire body to undergo atrophy.
- 4. The atrophy of the thymus gland at the age of puberty is a pathological atrophy.
- 5. The removal of a kidney results in a compensatory hypertrophy of the other kidney.

- 6. Hyperplasia is characterized by an increase in functional activity of a part.
- 7. Metaplasia is the conversion of epithelial tissue into connective tissue.

Completion Test

1. Atrophy of an organ may be due to a decrease in the ----- of cells or a decrease in the ----- of cells.
2. Atrophy of the female reproductive organs which accompanies the menopause is a ----- atrophy while that seen in a paralyzed limb is a ----- atrophy.
3. Hypertrophy is an effort of an organ or part to meet the increased demands made upon it by ----- activity.
4. Hypertrophy may be ----- as typified by the increased size of a blacksmith's arm or ----- as seen in the heart of a person suffering from a valvular heart lesion.
5. Metaplasia occurs most commonly in ----- and ----- tissues.

References

- Karsner, Howard T.: Human Pathology, Philadelphia, 1942, J. B. Lippincott Co.
- Forbus, Wiley D.: Reaction to Injury, Baltimore, 1943, Williams & Wilkins Co.
- Boyd, William: A Textbook of Pathology, Philadelphia, 1947, Lea & Febiger.
- MacCallum, W. G.: Textbook of Pathology, Philadelphia, 1940, W. B. Saunders Co.
- Moore, R. A.: Textbook of Pathology, Philadelphia, 1944, W. B. Saunders Co.

CHAPTER XLVII

TUMORS

Definition.—A tumor or neoplasm (Gr. *neos*, new, plus *plasma*, formation) is a special type of tissue growth of a destructive nature that serves no useful purpose and has **a tendency to increase in size and persist at the expense of the body.** This excludes purposeful growths such as those due to hypertrophy, inflammation, etc.

I. GENERAL CHARACTERISTICS OF TUMORS

The Cause of Tumors.—Of the cause of tumor growth we must yet confess our ignorance. Many theories have been proposed but they all remain theories. Perhaps when the problem is solved it will be found that there is no universal cause of tumors but that different kinds of tumors have different causes. Also, it will probably be found that many of these causes are preventable.

It seems fairly well proved that tumors arise from normal cells which have undergone a series of changes brought about by influences designated as intrinsic factors and that the changed cell is transformed into a tumor cell by the action of one or more influences known as extrinsic factors. By *intrinsic factors* are meant factors within the cells that become malignant or within the body as a whole. Among these are heredity, age, sex, endocrine influences and a natural predisposition to tissue overgrowth. By *extrinsic factors* are meant agents that originate without the body. The most important extrinsic factor is chronic irritation.

There seems to be some degree of predisposition to the development of tumors in certain families because for more than one hundred years recorded histories of such families has shown that the incidence of at least one group of tumors was greater in these families than in the population as a whole. Often the tumors affecting the members of such families were of the same type and affected the same organ. **Sarcomas** are more common in young people. **Carcinomas** are more common in those past adult life. Males are more

susceptible to certain kinds of tumors than females (ex., cancer of the stomach, mouth, lip, and lung), while females are more susceptible to certain other kinds (ex., cancer of the thyroid gland, urethra, and gall bladder). As a whole, it may be said that males are somewhat more susceptible to tumors than females when the organs peculiar to sex are excluded.

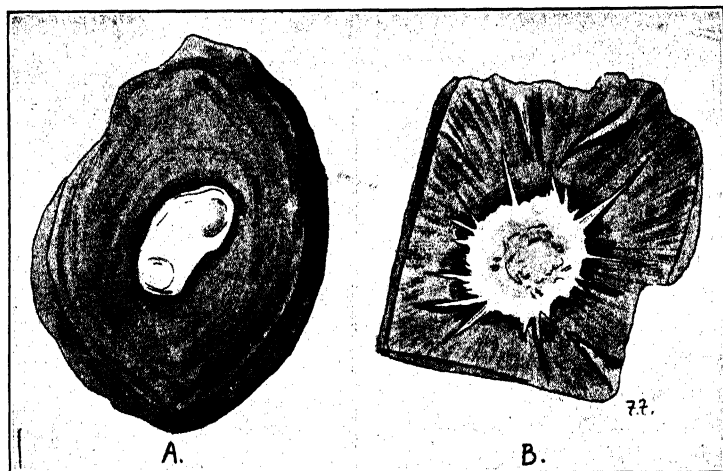


Fig. 142.—Comparison of expansive and infiltrative growth. *A*, Expansive growth; *B*, infiltrative growth. Tumor is represented by white. Note that in expansive growth the tumor mass is distinctly separated from the surrounding tissue which it is pushing aside. In infiltrative growth the tumor infiltrates the surrounding tissues and destroys them.

The most important excitant of tumor growth seems to be prolonged irritation. Such appears to be an important cause of cancer of the lip in pipe smokers and cancer of the cervix in women who have gone a long time with unrepaired cervical lacerations. In some cases it appears that transient non-destructive injuries as light blows sometimes precede sarcomas and gliomas, but careful investigation of such cases often reduces the apparentness of the relation. Experimental evidence indicates that filtrable viruses might be a cause of tumor growth in lower animals. The only tumor growth of man that has been experimentally produced by a virus is the ordinary wart. Agents that bring about the transformation of altered normal cells into the highly malignant type of

tumor cells known as carcinoma (cancer) cells are called *carcinogenic agents*. Important chemical carcinogenic agents are certain members of the coal tar group. These are used to produce cancer in the rabbit experimentally by repeatedly painting the ear. Carcinogenic agents are responsible for a number of occupational tumors. Among these are cancer of the skin in workers whose clothing is constantly soaked with mineral oil (mule spinners), and cancer of the bladder in those who work with aniline dyes.

The role of hormones in the production of cancer is being given considerable study at the present time. Cancer of the breast has been experimentally produced in mice by the injection of estrogenic substances, and several cases of cancer of the breast in human beings have been reported in which there appeared to be some relation between the tumor growth and the injection of estrogenic substances. The effect of reducing androgenic substances by castration or the injection of estrogenic substances is made use of in the treatment of prostatic cancer.

Resemblance Between Tumor Cells and Normal Cells.—

The cells of some tumors bear a close resemblance to normal cells, while in other tumors there is little resemblance to normal cells. As a rule the more the cells of a tumor differ from the cells of the tissue from which they arise, the more dangerous the tumor.

Environmental Control and Functions of Tumors.—The cells normally formed in the body are under complete environmental control. In tumors the cells are not under complete environmental control and they repeatedly multiply in an irregular and abnormal manner. If they have any function at all, it is abnormal and perverted. As Spencer has well said, cancer cells may be likened to ruthless gangsters who run amuck among the cells of an olderly functioning human economy.

Nourishment of Tumors.—While forming a part of the body, tumors are dependent upon it only for nourishment which they obtain regardless of the hardships which they impose. For instance, lipomas (tumors composed of fat) continue to grow after the body fat has been

almost depleted, and other tumors continue to develop even though the body is suffering from starvation.

The blood supply of tumors is obtained from the general circulation, and there may be an overdevelopment of vessels in the neighborhood of a tumor in order to meet the demands that the tumor makes. Occasionally the growth of a tumor is so rapid that the blood supply is incapable of keeping up with it, and the tumor undergoes necrosis, which is followed by infection, sloughing, and hemorrhage.

Mode of Growth of Tumors.—Tumor growth may be expansive or infiltrative. In the former the tumor grows from its center and pushes the surrounding tissues aside but does not invade them. In the latter, growth takes place from the periphery of the tumor and strands of cells grow out into the surrounding tissues and destroy them. Tumors growing by expansion are circumscribed, encapsulated and sharply separated from the surrounding tissues. Those growing by infiltration are nonencapsulated and grade off imperceptibly into the surrounding tissues. The method by which a tumor grows has a most important bearing on its benign or malignant qualities.

Resistance of Tumor Cells.—The cells of tumors have little resistance to destructive influences and little reparative ability and for this reason tumors, especially those of the skin, often show early ulceration and extensive necrosis. Ulceration may involve large blood vessels and lead to severe hemorrhage.

II. CLASSIFICATION OF TUMORS

A satisfactory classification of tumors is a very difficult matter. For anything like a comprehensive knowledge it is necessary to classify them from both the clinical and histological standpoint. The latter refers to the origin and nature of the cells of which the tumor is composed.

From the clinical standpoint tumors are classified as *malignant* and *nonmalignant* (innocent or benign). The characteristics of each type will be given in subsequent paragraphs.

In the histological classification a tumor is designated by adding the suffix “oma” to the name of the tissue from which the tumor originated. For instance, myoma means a

tumor originating from muscle tissue. In tumors derived from connective tissue or muscle the suffix "oma" is reserved for nonmalignant tumors, while the malignant tumors are designated by the suffix "sarcoma." For instance, an osteoma would be a benign tumor originating from bone while an osteosarcoma would be a malignant tumor originating from bone.

The following classification does not include all tumors but it has the advantage that it is very simple. In connection with any classification it should be remembered that fat, cartilage, bone, and vascular tissue are but specialized types of connective tissue.

I. Arising from Epithelium	Benign	<ul style="list-style-type: none"> Papilloma Adenoma
	Malignant (Carcinomas)	<ul style="list-style-type: none"> Squamous cell or epidermoid carcinoma Adenocarcinoma Carcinoma simplex
II. Arising from Connective Tissue	1. Unmodified Connective Tissue	<ul style="list-style-type: none"> Benign—fibroma Malignant—sarcoma
	2. Fat	<ul style="list-style-type: none"> Benign—lipoma Malignant—liposarcoma
	3. Cartilage	<ul style="list-style-type: none"> Benign—chondroma Malignant—chondrosarcoma
	4. Bone	<ul style="list-style-type: none"> Benign—osteoma Malignant—osteosarcoma
	5. Blood or Lymph Vessels	<ul style="list-style-type: none"> Benign—angioma Malignant—angiosarcoma
	6. Mucous Tissue	<ul style="list-style-type: none"> Benign—myxoma Malignant—myxosarcoma
III. From Muscle Tissue	1. Smooth Muscle	<ul style="list-style-type: none"> Benign—leiomyoma Malignant—leiomyosarcoma
	2. Striated Muscle	<ul style="list-style-type: none"> Benign—rhabdomyoma Malignant—rhabdomyosarcoma
IV. From Nerve Tissue	1. Glioma—from the supporting tissue of the nervous system	
	2. Neuroma—from functioning nerve tissue	

- V. From Lymphoid Tissue—Lymphoma and lymphosarcoma
- VI. From Endothelium—Endothelioma
- VII. Pigmented Tumors { Nonmalignant—nevus
 { Malignant—melanoma
- VIII. From Adrenal Tissue—Hypernephroma
- IX. From Chorionic Villi—Chorionepithelioma
- X. Complex Tumors { Mixed tumors
 { Dermoids
 { Teratomas

III. BENIGN TUMORS

There are seven outstanding characteristics of benign tumors:

1. They grow by expansion and do not infiltrate the surrounding tissues.
2. They do not spread to other parts of the body by the blood and lymph and produce secondary growths (metastasis).
3. They do not recur when removed.
4. They do not cause extensive destruction of tissue.
5. They do not produce such general effects on the body as anemia, weakness, loss of weight, etc.
6. As a rule, their cells resemble the normal cells of the tissue from which the tumor arose.
7. They do not kill except when situated in such locations that they interfere with vital organs.

The slow expansive growth of the tumor with its pressure on the surrounding tissues leads to the formation of a *capsule*. The capsule represents a reaction on the part of the surrounding tissues and is a part of them, not of the tumor. Benign tumors are made up of normal adult tissue or tissue bearing a close resemblance to it. They do not undergo degenerative changes as often as malignant tumors. Benign tumors which produce death by interfering with the activities of vital organs are spoken of as being "*malignant by position*." For example, a tumor of considerable size, regardless of its nature, growing in the cranial cavity will eventually lead to death of the host by pressing upon the

brain. Benign tumors may produce disturbances of remote organs by pressing upon the vessels or nerves supplying them.

A. Benign Epithelial Tumors

Benign epithelial tumors may arise from any location where epithelium is found.

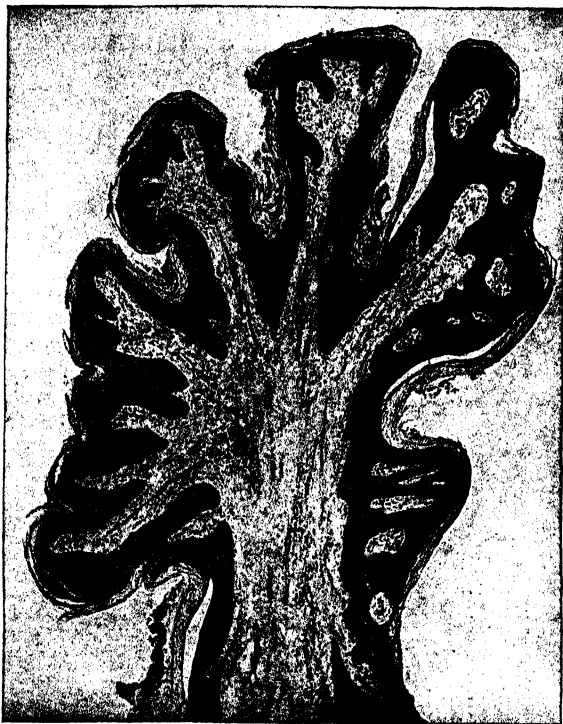


Fig. 143.—Papilloma of skin, showing thickened epithelium covering a central connective tissue core. (From Woolley: *Fundamentals of Pathology*.)

Papillomas are cauliflower-like, epithelium-covered projections which spring from the skin or mucous membrane. Those that are covered with stratified squamous epithelium are known as *hard papillomas* or *warts*. They arise most often from the skin or mucous membrane of the mouth or larynx. The warts seen on the hands of children are known as *verruca vulgaris*. They are generally regarded as being

of an infectious nature. Papilloma of the larynx often occurs in children and has a tendency to disappear at puberty but it may become malignant. Papillomas covered with epithelium other than the stratified squamous type are known

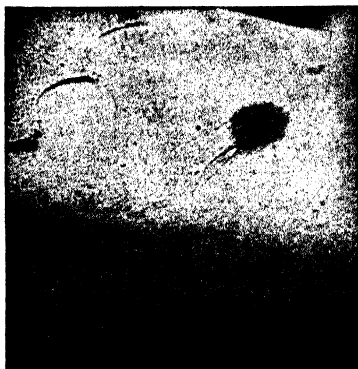


Fig. 144.—Pigmented nevus. (From Sutton and Sutton: *Diseases of the Skin*. The C. V. Mosby Co.)



Fig. 145.—Pigmented nevus; "bathing trunk" type. (From Pack and Anglem: *J. Pediat.* 15: 372, 1939.)

as *soft papillomas*. They occur most often in the intestinal canal and bladder. Soft papillomas, especially those of the bladder, are likely to become malignant. *Acuminate condylomas* (pointed or venereal warts) are moist papillomatous

processes which occur around the genitalia as a result of irritating discharges. They are especially common in gonorrhea. *Condyloma latum* is a broad flat papillary process which occurs about the anus in syphilis. *Cutaneous horns* are epithelial overgrowths seated on a papillary base.

Adenomas are tumors which are made up of glandular structures and are derived from tissues of a glandular nature, such as the breast or prostate.

Cystadenomas result when one or more of the glands of an adenoma enlarge and become cystic. This is usually due to a retention within the glands of their own secretion. Cystadenomas are of two types: pseudomucinous and serous. The former are so frequently multilocular (made up of more than one cavity) and the latter have papillary growths within them so often that they are also spoken of as multilocular and papillary cystadenomas respectively. The *pseudomucinous cystadenoma* consists of several cystic spaces filled with a stringy viscid material. The *serous* or *papillary* cystadenoma usually consists of one cavity from the lining of which treelike papillary growths extend into the cavity or penetrate the wall of the cyst and grow externally. Although papillary cystadenomas are here considered with the benign tumors, they are extremely prone to malignant changes and often recur after removal. Both types of cystadenomas are of frequent occurrence in the ovary. Cystadenomas of the breast are of the papillary type.

Pigmented nevi (pigmented moles) are small dark or brown pedunculated or nonpedunculated structures which occur especially about the neck and face. Nevi are often covered with coarse hair. In a few cases the nevus covers a considerable area, e.g., the "bathing trunk" nevus. They are composed of aggregations of peculiar cells known as nevus cells which lie beneath the epithelium. These cells contain a brown pigment, melanin, which gives the tumors their color. Nevi are usually congenital, but they may not be noticed until some time after birth. As a rule they remain stationary or regress, but occasionally they develop marked

growth capacities and give rise to highly malignant tumors (melanomas). This usually follows an injury or injudicious surgical removal.

B. Benign Connective Tissue Tumors

Fibromas are benign tumors made up of connective tissue. Considering the wide distribution of connective tissue, fibromas are infrequent. They occur most often in the skin, mucous membranes, and muscles. They are usually round or nodular and encapsulated and are frequently attached to the point of origin by a pedicle. Nasal polyps are soft pedunculated fibromas.

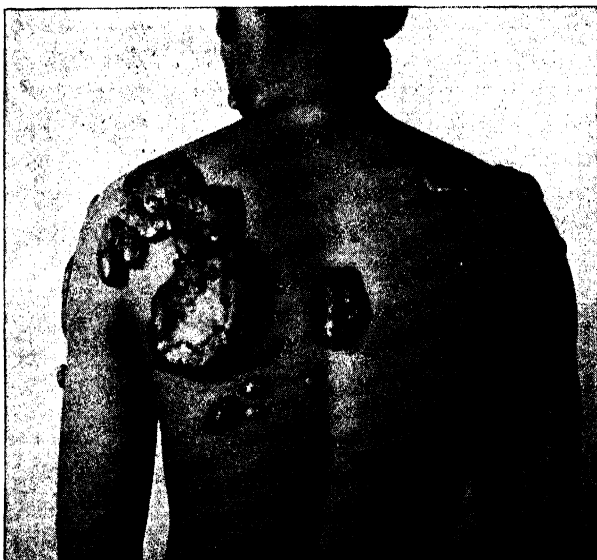


Fig. 146.—Keloids. (From Anderson: Synopsis of Pathology.)

Keloid is not a true tumor but consists of an overgrowth of the dense connective tissue of scars. It occurs most often following burns.

Lipomas are tumors composed of fat. In the ordinary sense they are the most benign of all tumors, but they may cause serious disturbances on account of their large size. Lipomas occur chiefly in the subcutaneous tissues of the

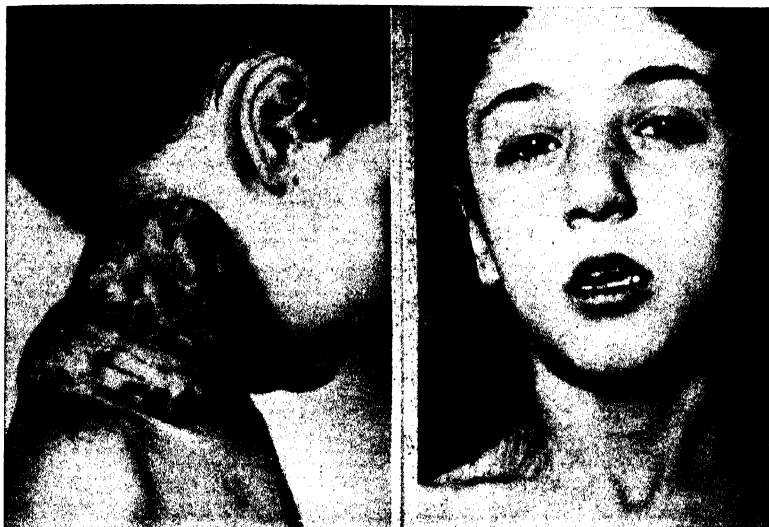


Fig. 147.—*Left*, Large hemangioma of neck. *Right*, Result obtained by surgical removal. (From Watson: *J. Pediat.* 15: 401, 1939.)

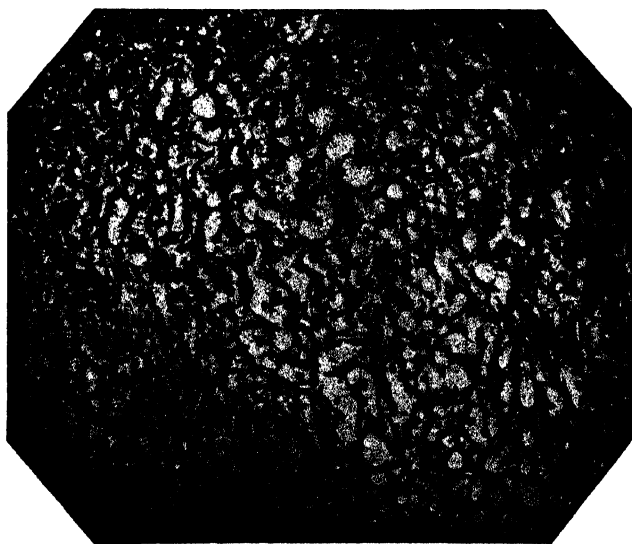


Fig. 148.—Microscopic section of angioma. The clear spaces are blood vessels. Some angiomas are composed of lymph vessels. (From Woolley: *Fundamentals of Pathology.*)

neck, shoulders, and buttocks, but may occur wherever adipose (fat) tissue is found. They are usually round, lobulated, surrounded by a thin capsule, and are removed with ease.

A *chondroma* is a tumor composed of cartilage. Chondromas occur most often in connection with bones, especially long bones and the bones of the hands and feet. They also form a part of certain mixed tumors.

Osteomas are benign tumors composed of bone. It is often difficult to differentiate true osteomas which are comparatively rare from certain inflammatory or traumatic bony overgrowths which are rather common. True osteomas usually occur in connection with the bones of the face, most often those of the nasal sinuses and orbit. Other tumors sometimes undergo secondary ossification. This is most frequent in fibromas, lipomas, and certain sarcomas.

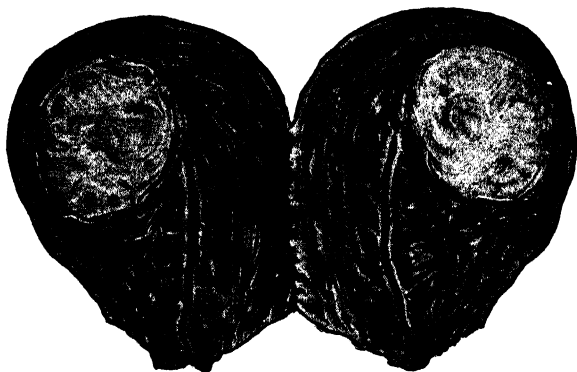


Fig. 149.—A myoma in the wall of the uterus. The uterus has been sectioned longitudinally. (From Crossen and Crossen: *Diseases of Women*. The C. V. Mosby Co.)

Angiomas are tumors composed of newly formed blood or lymph vessels. If composed of blood vessels they are known as *hemangiomas*; if composed of lymph vessels they are known as *lymphangiomas*. Angiomas are to be differentiated from telangiectases (dilatations of capillaries already present).

Capillary hemangiomas consist of a network of capillaries. *Cavernous* hemangiomas consist of large communicating blood spaces. The most common site of capillary hemangio-

mas is the skin, especially the skin of the face. They may cover a considerable area and are spoken of as "birth-marks," "strawberry marks" or "port wine stains" (see page 572). They consist of a sheet of thin-walled capillaries lying just beneath the superficial layer of the skin. Birth-marks may ulcerate and be replaced by scar tissue. Cavernous hemangiomas are most often found in the liver. They are elevated, have a bluish color, and may be emptied by pressure. Marked hemorrhage may attend attempts to remove them.

Capillary lymphangiomas occur on the skin as colorless moles. The cavernous form may produce a diffuse enlargement of the tongue (macroGLOSSIA) or lip (macrocheilia).

C. Benign Tumors Composed of Muscle Tissue

A *myoma* is a tumor composed of muscle tissue. There are two types: *leiomyomas* derived from smooth muscle and *rhabdomyomas* derived from striated muscle. The former is one of the most common tumors and the latter is one of the most rare. Leiomyomas are of importance on account of their growth in connection with the uterus. Here the muscle cells have associated with them actively growing connective tissue cells so that histologically the tumor must be classified as a *fibromyoma* or *myofibroma*.

D. The Transformation of Benign Into Malignant Tumors

Although the transformation of benign into malignant tumors is often talked about, in reality it seldom occurs. In fact it is more likely that a malignant tumor will arise from the heretofore normal tissues of an organ than it is that a benign tumor in the same location will become malignant. It must be admitted, however, that certain benign tumors or tumorlike growths have a tendency to become malignant. For instance, fibromyomas of the uterus and fibroadenomas of the breast may become sarcomas, while certain polypoid tumors of the stomach, intestines, and rectum may become cancers. So likely are tumors of the bladder to become malignant that there is a tendency on the part of pathologists to regard all bladder tumors as potentially malignant.

IV. MALIGNANT TUMORS

A *malignant* tumor is one whose tendency is to spread widely, set up secondary foci in other parts of the body, and kill regardless of location. The two most important groups of malignant tumors are the *carcinomas* (cancers) of epithelial origin, and the *sarcomas* of connective tissue origin. There are certain characteristics which identify a tumor as malignant. Naturally they are the opposite of those which identify it as benign.

1. They grow chiefly at the periphery where they send out processes to infiltrate and destroy the surrounding tissues.

2. Cells of the tumor gain access to the lymph and blood stream by which they are transported to different parts of the body, where secondary tumors are produced (metastasis).

3. They often recur when removed.

4. They cause extensive destruction of tissue.

5. They produce general effects on the body such as anemia, weakness, loss of weight, etc.

6. Their cells often have little resemblance to the normal cells of the tissue from which the tumor arose.

7. Unless they are properly treated they kill regardless of location.

The cells of malignant tumors are of an immature type and have the capacity to multiply rapidly. This is why malignant tumors usually grow more rapidly than benign tumors. The arrangement of the cells in the tumor does not conform to that of any normal tissue, while benign tumors often have a striking resemblance to normal tissue.

Malignant tumors spread chiefly by invasion of the surrounding tissues and by metastasis. Occasionally they spread by contact or implantation. By *metastasis* is meant the transfer of cells from the tumor to other parts of the body where they lodge, multiply, and produce other tumors. Metastasis by the lymph stream is usually regional; i.e., to the lymph nodes draining the area. The lungs and liver are the most common sites of secondary growths when metastasis occurs

by the blood stream. Sarcomas usually metastasize by the blood stream, carcinomas usually metastasize by the lymph stream.

When metastasis occurs by way of the lymph stream, the tumor cells first lodge in the lymph nodes which receive their drainage directly from the tumor site. These nodes hold the cells in check for a time but finally the cells gain the upper hand and by their multiplication destroy the nodes and replace them by a tumor mass. Tumor cells then escape to the next set of nodes, and the process is repeated. This continues until the last lymphatic barrier has been overcome,

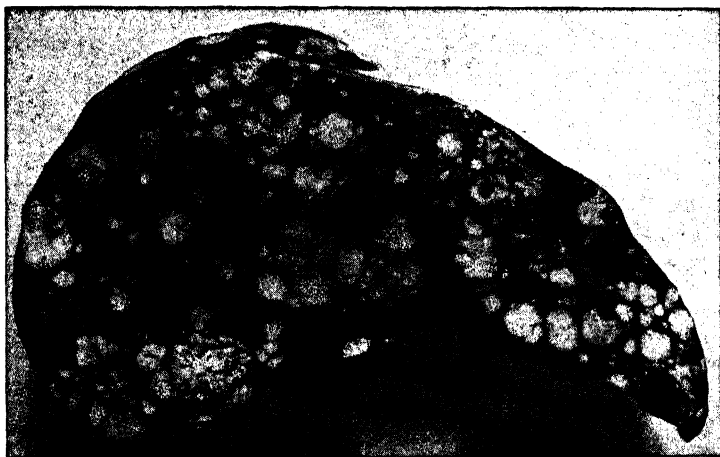


Fig. 150.—Metastatic carcinoma of liver. The white nodules are growths of tumor tissue. The primary tumor was in the stomach. (From Anderson: Synopsis of Pathology.)

and the cells pass to the blood stream by way of the thoracic duct to be spread to remote parts of the body. This explains why it is necessary when removing a malignant growth that metastasizes by the lymphatics to remove also as completely and extensively as possible the lymph nodes which receive drainage from the tumor site.

To a great extent metastatic tumors retain the characteristics of the parent tumor. Some tumors metastasize early in their course while in others metastasis is late. Occasion-

ally metastasis may be far advanced before the primary tumor is clinically perceptible.

Table II gives the points of metastasis of the more frequently encountered tumors.

TABLE II

TUMOR	POINT OF METASTASIS
1. Cancer of the Breast	Regional lymph nodes and bones
2. Cancer of Stomach and Intestines	Liver
3. Cancer of Uterus	{ Cervix: bladder, vagina, rectum and pelvic lymph nodes Body: regional lymph nodes and ovary
4. Cancer of Prostate Gland	Bones
5. Cancer of Lip	Lymph nodes of neck
6. Cancer of Mouth	Lymph nodes of neck
7. Melanoma of Eye	Liver
8. Sarcoma (bone)	Lungs
9. Cancer of Thyroid Gland	Bones
10. Carcinoma of Kidney	Bones
11. Hypernephroma	Bones

The complete removal of a malignant tumor is extremely difficult. From a practical standpoint a tumor may be considered cured if it does not recur within five years after treatment.

A. Malignant Epithelial Tumors

We now come to the most interesting of all tumors, the carcinomas or cancers, which are among the most common tumors affecting persons above thirty-five years of age. They are by no means rare in younger persons and when occurring in young people are more highly malignant than in older persons.

Since epithelial cells form the superficial layers of the skin and mucous membranes as well as the active tissues of many organs and the lining of glands, it follows that carcinomas may occur in almost any part of the body. With the exception of the lungs, in which both primary and secondary carcinomas are common, organs which are often the site of primary carcinomas are seldom sites of metastatic carcinomas and vice versa.



Fig. 151.—Carcinoma of finger. (From Anderson: Synopsis of Pathology.)

TABLE III

FREQUENTLY THE SITE OF PRIMARY CARCINOMA, SELDOM THE SITE OF SECONDARY CARCINOMA	FREQUENTLY THE SITE OF SECONDARY CARCINO- MA, SELDOM THE SITE OF PRIMARY CARCINOMA	SELDOM THE SITE OF CARCINOMA EITHER PRIMARY OR SEC- ONDARY
Stomach	Lymph nodes	Spleen
Breast	Liver	Heart
Pancreas	Pleura	Skeletal muscle
Prostate	Bone marrow	

Table III shows the susceptibility of organs to cancer.

Carcinomas usually spread by invasion of the lymphatics and by the outgrowth of branching extensions from the tumor which invade and destroy the surrounding tissues. The method of lymphatic spread was discussed under the heading of Metastasis.

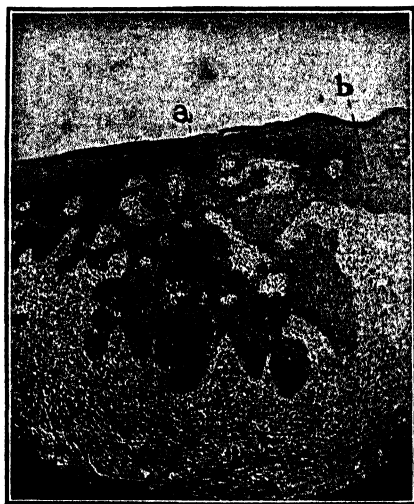


Fig. 152.—Microscopic section of epithelioma of skin. *a*, epithelium growing into and destroying underlying tissue; *b*, normal epithelium limited by a definite basement membrane. (From Sutton and Sutton: *Diseases of the Skin*. The C. V. Mosby Co.)

A simple classification of carcinomas is as follows:

1. *Epithelioma* (squamous cell carcinoma or epidermoid carcinoma), arising from stratified squamous epithelium.
2. *Adenocarcinoma*, arising from glands and producing glandular structures.

3. *Carcinoma simplex*, arising from glands and producing strands and plugs of epithelial cells instead of glandular structures.

Epitheliomas occur at any point where stratified squamous epithelium is found. Adenocarcinomas are most common in the breast, alimentary canal, and uterus. Carcinoma simplex occurs most often in the breast.

Carcinomas occur as cauliflower-like growths, a diffuse hardening of the tissues, or as ulcers. The scarring produced by certain internal carcinomas may be apparent on the surface; e.g., the retraction of the nipple in cancer of the breast. Regardless of position, carcinomas usually undergo ulceration or infection and the patient dies of sepsis or pneumonia.

Epitheliomas are most common in the cervix uteri, on the skin (especially on the lip), and in the mouth. Normally the downgrowth of the covering epithelium is limited by a structure known as the basement membrane. In epitheliomas the cells break through this barrier, invade the underlying tissues, and destroy them. Epithelioma of the cervix uteri is discussed on page 722, and epithelioma of the lip and mouth is discussed on page 643.

Rodent ulcers (basal cell carcinomas) differ from epitheliomas in that they are of a different structure, do not grow rapidly, and do not metastasize. They occur most often in the region of the nose and eye. They are shallow ulcers that may spread in one portion while they are healing in another.

Carcinoma of the Breast (see page 727).

Carcinoma of the Body of the Uterus (see page 723).

Carcinoma of the Lung (see page 618).

Chorionepithelioma (see page 724).

B. Malignant Connective Tissue Tumors

Sarcomas are malignant tumors of connective tissue origin. The cells of sarcomas seem to have the quality of lawless multiplication, more highly developed than those of any other tumor. Sarcomas are malignant on account of both their invasive growth and the formation of metastases.

Being of connective tissue origin sarcomas are likely to occur in any part of the body. They are more common in early life but may occur in the aged. Growth may be slow

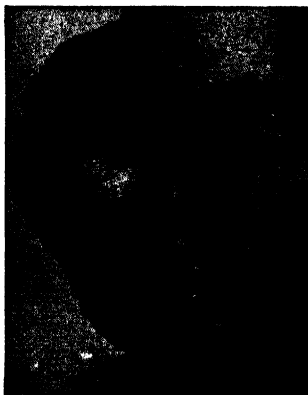
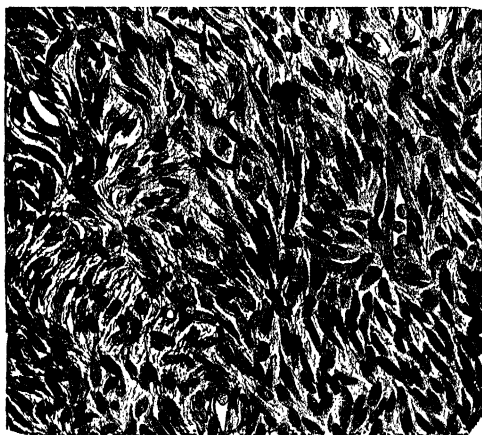


Fig. 153.—Sarcoma of the face. (From Sutton and Sutton: *Diseases of the Skin*.)



154.—Microscopic section of spindle cell sarcoma. Note that the tumor is composed almost entirely of spindle-shaped cells. (From Karsner: *Human Pathology*. J. B. Lippincott Co.)

at first and then rapid, or it may be rapid from the beginning. Sarcomas are soft, bulky tumors of a white, gray or pink color, and have an abundant blood supply. They are usually single but may be multiple. Growth of the tumor may be so rapid that it outstrips that of its blood supply

which results in degenerative changes and hemorrhage. This is of such frequency that a hemorrhage in a tumor should lead to a suspicion of its sarcomatous nature. The cells of sarcomas show marked variation in size but are usually round or spindle-shaped. Sarcomas differ from carcinomas in that they metastasize widely by way of the blood stream. Secondary growths occur most often in the lungs and liver.

The giant cell tumors of bone are often spoken of as "giant cell sarcomas" but "giant cell tumor" is the better term because the term "sarcoma" suggests a highly malignant tumor while giant cell tumors are comparatively benign. In fact some workers regard them as not being tumors but of inflammatory origin. There is, however, a sarcoma in which there are multinucleated giant cells of a different type from those of giant cell tumor. This tumor is highly malignant. Giant cell tumor is further discussed on pages 644 and 754.

C. Other Malignant Tumors

Gliomas arise from neuroglia, the supporting tissue of the nervous system. They occur in the brain and in the retina. They do not metastasize but kill by local invasion and destruction. *Neuroblastomas* are rare tumors composed of nerve cells. Peculiarly they occur more often in the adrenals than in the central nervous system.

Endotheliomas are tumors derived from endothelium. In the light of our present knowledge many tumors previously classed as endotheliomas are now placed in other groups.

Melanomas are highly malignant brown or black pigmented tumors which usually arise from pigmented nevi but may arise from other locations, especially the eye. Why most pigmented nevi remain quiescent throughout life while a few give rise to highly malignant tumors has not been satisfactorily explained. In many cases accidental injury or injudicious surgical removal seems to be the spark that sets off the conflagration. In most cases the primary growth remains insignificant while metastasis is widespread and destructive. Secondary melanotic foci usually appear first in the skin. The spread continues rather rapidly until the lungs, kidneys, and other organs become studded with tumor

growths. Melanin, the pigment which gives the tumors their color, may appear in the urine.

Hypernephromas (see page 694).

Lymphomas are tumors composed of lymphoid cells (the cells of which the lymph nodes are composed). One type of importance are those associated with leucemia. Others are true malignant tumors (lymphosarcomas). Lymphomas and lymphosarcomas are frequently difficult to differentiate from inflammatory lymphadenopathies.

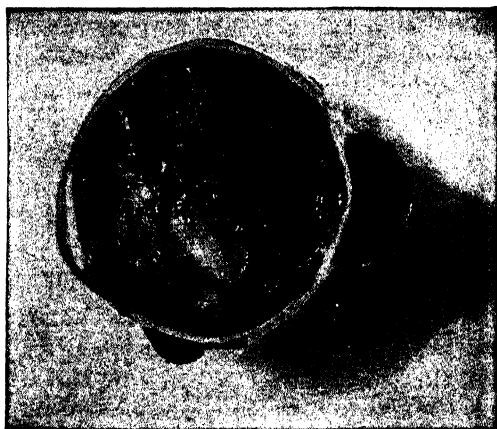


Fig. 155.—Malignant melanoma of eye. The black tumor mass almost fills the eye and is breaking through its wall. (From Anderson: *Surgery* 9: 425, 1941.)

D. Estimating the Malignancy of a Tumor

In estimating the malignancy of a tumor, the following characteristics of the tumor must be considered: (1) kind of tumor, (2) location, (3) extent of local growth and occurrence of metastasis, (4) rate of growth, (5) age of patient, and (6) microscopic appearance of tumor.

Some tumors are naturally more likely to cause death than are others. Malignant melanomas usually cause death regardless of treatment, while a rodent ulcer (basal cell carcinoma) may exist for years without causing death, even if no treatment is given. Tumors in some locations are more likely to cause death than the same kind of tumor occurring in another location. For instance a squamous cell carcinoma

arising from a keratosis on the face is much less likely to cause death than one arising on the hand or foot. Extensive tumors are of greater danger than ones confined to a restricted area. Prognosis is poor if the tumor has undergone metastasis and increasingly poor with the extent of the metastasis. As a rule, fast-growing tumors are more dangerous than slowly growing ones, but this is not always true. In some tumors the young succumb more quickly than the aged.

Broders, of the Mayo Clinic, has devised a method of grading tumors based on histological grounds in which, in order of malignancy, the tumor is placed in grades 1, 2, 3, and 4. This method is of distinct value.

E. Economic Importance and Value of Early Diagnosis in Malignant Tumors

When we realize that in the registration area of the United States there are almost 500,000 malignant tumors with an annual death rate of more than 150,000, and that about 300,000 new cases are being diagnosed each year, their economic importance becomes apparent. At the present time malignant tumors are the second most important cause of death, and the death rate is increasing about 2 per cent annually. The idea that cancer is primarily a disease of late life has done much to prevent its early recognition. Let us remember that while cancer is most common in the latter decades it is by no means uncommon in early life and its frequency during this period seems to be increasing.

Since the cause of tumors is unknown, any discussion of their prevention must deal with unknown factors. The only practical weapons to stem the rising tide of malignant tumors now at our command are prevention, early recognition, correct diagnosis, and proper treatment applied early. The close relation which the nurse bears to the physician, the patient, and the patient's family often places her in such a position that she is of inestimable aid in the consummation of the above requisites upon which the control of malignant tumors rests. For this reason she should be in possession of the general facts on which this control rests, and she should also be familiar with those signs and symp-

toms which indicate beginning malignancy in the different organs. In the following paragraph we shall attempt to outline these essential facts. They refer particularly to the type of malignant tumors known as cancers, for this is the type most frequently encountered.

1. General Facts.—Statistics show that the average patient waits eight months after first suspecting a malignant condition before consulting a physician, and that with some tumors each month of delay decreases the chances of cure 16 per cent.

Many tumors appear to bear a definite relation to one of the various types of chronic irritation to which the body is continually exposed. To prevent this exposure is to prevent cancer.

The method which more than any other will bring to light beginning tumors is a periodic physical examination by a competent physician. It should be carried out at least once a year and in women it should include a pelvic examination.

2. Cancer of the Skin.—Warts which show an increase in growth or other signs of activity should be treated to prevent their becoming malignant. Signs of beginning malignancy in pigmented moles are increase in size and in amount of pigment. Scaly, small pigmented patches about the face of old people are likely to become malignant. Weeping sores and those which continuously break down, scab, and heal are usually malignant. An ulcer which refuses to heal after a period of three weeks should be investigated to determine its malignant or nonmalignant nature. Workers in crude oil, paraffin, tar, arsenic, radium, and x-ray are prone to develop cancer of the skin.

3. Cancer of the Lip and Mouth.—Cancer of the mouth and lip often follows such chronic irritations as those caused by dental irregularities, buccal decay, chronic infections, tobacco, pipe stems, etc. Cancer of the lip usually begins as a localized pearly thickening or wartlike outgrowth. It almost always occurs on the lower lip. Broken, out of line, and sharp-edged teeth often bring about a chronic irritation of the buccal cavity which ends in cancer. Leucoplakia

("white spot disease") often ends in cancer. Cancer of the lip and mouth are of extreme importance because metastasis occurs early.

4. Cancer of the Breast.—The first sign of cancer of the breast is usually a painless lump which is often found by accident. In a few cases the first sign is bleeding from the nipple. The fact that 70 per cent of women who receive early treatment are alive at the end of five years, while only 4 per cent of those who are treated late are alive at that time is proof of the importance of early diagnosis and treatment. If one breast is removed for cancer, the one remaining should not be subjected to lactation.

5. Cancer of the Uterus.—Cancer of the uterus is more common in women who have had children, and it arises most often at the site of an old cervical laceration. The major preventive procedure, therefore, becomes the proper repair of lacerations at childbirth.

The first sign of uterine cancer is usually a blood-tinged watery discharge which at first may appear only on exertion. This is followed by frank bleeding which may occur in the form of (1) excessive menstruation, (2) intermenstrual bleeding, or (3) bleeding after the menopause. Any bleeding after the menopause should be assumed to be caused by cancer until proved otherwise; in 90 per cent of cases the assumption will be found to be correct. Profuse bleeding indicates an advanced condition. The commonly believed fallacy that the menopause is accompanied by irregular bleeding has done much to retard the early recognition of uterine cancer. The only safeguard against cancer of the uterus is the periodic pelvic examination of all women past thirty years of age. This is particularly true in the case of women who have had children.

6. Cancer of the Stomach.—The first sign of this disease is often a persistent unexplained indigestion and lack of appetite, especially for meats, with a peculiar disturbance of taste.

7. Cancer of the Intestines.—Intestinal cancer usually begins with a vague abdominal distress which increases to pain, at first intermittent then constant.

8. Cancer of the Rectum.—Rectal cancer is very often misdiagnosed as constipation or hemorrhoids. Most valuable time is thereby lost. Blood in the stool is often the sign which directs the patient's attention to his condition.

9. Tumors of the Urinary Tract.—Blood in the urine is often the sign which arouses the patient's interest. Every case of hematuria (blood in the urine) should be thoroughly investigated.

10. Tumors in Children.—Tumors are infrequent in children but they do occur. The parts most frequently involved are the bones and kidneys. In bone tumors pain followed by enlargement is the important symptom. In kidney tumors bloody urine and abdominal tumor are the early signs.

F. The Principles of the Radiation Therapy of Malignant Tumors

The fundamental principle of the radiation (x-ray and radium) therapy of malignant tumors is that the cells of malignant tumors are poorly developed cells and are, therefore, destroyed by radiation doses that have little effect on the normal cells of which the body tissues are composed. The more rapidly a tumor is growing the more easily are its cells destroyed by radiation. Certain types of cells are more easily destroyed by radiation than others. In order of their sensitivity to radiation, cells and tissues may be classified as follows: (1) lymphoid tissue, (2) polymorphonuclear leucocytes, (3) epithelial cells (varying according to structure and location), (4) endothelial cells, (5) connective tissue, (6) muscle, (7) bone and (8) nerve tissue.

Although rapidly growing tumors are more sensitive to radiation than slowly growing ones, it is not necessarily true that the more malignant a tumor is the more sensitive it is to radiation. For instance, certain melanomas are highly malignant but not sensitive to radiation while myelomas are less malignant but much more sensitive to radiation than melanomas.

G. Cause of Death in Malignant Tumors

The death of a person who has a malignant tumor is often caused by associated or intercurrent conditions instead of

by the primary effects of the tumor itself. Among these associated or intercurrent causes are bronchopneumonia (the most common cause), other pulmonary conditions, cachexia, spread of the tumor to vital organs, the general spread of the tumor over the body, obstruction of the natural passages of the body (tumors of the intestine, bladder, etc.), and renal failure.

V. TERATOMAS

Teratomas are complex tumors composed of irregularly arranged tissues which may represent several different organs. They are due to errors in development and may be regarded as attempts to form a new individual within the tissues of the parent. A study of fetal development will show that there is a descending relation existing between identical twins, double monsters, parasitic fetuses, and teratomas. Teratomas occur chiefly in the ovary and testicle.

Teratomas of the ovary are known as dermoid cysts. They are discussed on page 713.

Teratomas of the testicle may be comparatively benign but they have a great tendency to become highly malignant. As a rule they form rather bulky tumors and completely destroy the testicle. Malignant changes may affect any of the tissues so that the tumor may metastasize as a carcinoma, sarcoma, or other type of tumor. Teratomas are most frequent in undescended testes.

Closely related to the teratomas but of a simpler nature are the mixed tumors of the salivary glands and kidneys.

VI. CYSTS

Cysts are sacs which contain a material different from that composing the wall. The wall is most often connective tissue, and the contents are most often a liquid.

Cysts have no special relation to tumors other than that certain tumors may be cystic or the walls of certain cysts may give rise to tumors.

Cysts which are composed of one compartment are known as *unilocular* cysts; those which are composed of several compartments are known as *multilocular* cysts.

Some cysts are congenital and may be due to the persistence of ducts which normally disappear or to other errors

of development. Such cysts may be found in the neck or in connection with the genitourinary tract. Congenital cysts may also occur in the liver and kidney.

Retention cysts are due to the occlusion of the duct of a gland with retention of secretions. A good example is the sebaceous cyst or wen which is due to the occlusion of the mouth of a sebaceous gland. Follicular cysts are due to the oversecretion of glandular structures which do not have a duct. The best example is the follicular cyst of the ovary.

Localized necrosis and softening of solid organs may lead to the formation of cystlike structures known as *pseudo-cysts*. Cysts may be associated with the growth of certain parasites. The only one of this type that is of importance in man is the echinococcus cyst due to a type of tapeworm, *Echinococcus hominis*. Cysts are sometimes a part of certain tumors. These are known as neoplastic cysts.

Questions for Review

1. Define a tumor.
2. What are the predisposing causes of tumors?
3. What is the origin of tumor cells?
4. From what source do tumor cells obtain their nourishment?
5. How are tumors classified from a clinical standpoint? From a histological standpoint?
6. What are some outstanding characteristics of benign tumors?
7. Give three examples of benign tumors of epithelial origin.
8. What are the following: keloid, chondroma, teratoma, dermoid cyst?
9. What are some outstanding characteristics of malignant tumors?
10. What are the chief signs of malignancy?
11. What is meant by metastasis?
12. Why are the lymph nodes of the axillary region removed when a radical breast operation for carcinoma is done?
13. Name the three classes of carcinomas.
14. What is a rodent ulcer?

True-False Test

Place the word "true" or "false" before each statement.

- 1. A tumor is a group of new cells in the body which grow independently of the rest of the tissues.
- 2. Tumor cells are characterized by disorderly growth.
- 3. The less resemblance tumor cells have to normal body cells the less malignant they are.

- 4. Malignant tumors are at first local but do not remain so.
- 5. The way a tumor grows determines whether it is benign or malignant.
- 6. Benign tumors may produce death.
- 7. A benign tumor often transforms into a malignant tumor.
- 8. The malignancy of carcinomas increases with age.
- 9. Carcinoma is largely a disease of old age but no age is free from it.
- 10. Sarcomas, as a rule, occur in older people than carcinomas.
- 11. Carcinoma of the liver is rarely a primary tumor but is often secondary to carcinoma of the stomach.
- 12. Children are not susceptible to carcinoma but frequently have sarcomas.
- 13. Birthmarks are tumors composed of blood vessels lying just beneath the skin.
- 14. The capsule which usually surrounds a benign tumor is a part of the tumor itself.
- 15. Rapidly growing tumors are always more sensitive to radiation than slowly growing ones.

Completion Test

1. Carcinomas develop from ----- tissue and metastasize through the -----; sarcomas are of ----- tissue origin and metastasize through the ----- stream.
2. Malignant tumors grow by ----- and ----- the surrounding tissues; benign tumors grow by ----- and ----- the surrounding tissues.
3. Fibroids are ----- tumors of the muscle and ----- tissue of the uterus.
4. A benign tumor of fat is a -----, of the bone is an -----, of blood vessels is an -----; a malignant tumor of fat is called a -----, of bone is called an -----, of blood vessels is called an -----.
5. Nevi are ----- which have a tendency to become ----- especially when subjected to -----.
6. A wart is a ----- or a ----- tumor.

References

- Boyd, William: A Textbook of Pathology, Philadelphia, 1947, Lea & Febiger.
- Boyd, William: Surgical Pathology, Philadelphia, 1947, W. B. Saunders Co.
- Ewing, James: Neoplastic Diseases, Philadelphia, 1940, W. B. Saunders Co.
- Stout, Arthur P.: Human Cancer, Philadelphia, 1932, Lea & Febiger.
- Sutton and Sutton: Diseases of the Skin, St. Louis, 1939, The C. V. Mosby Co.

- Behan, R. J.: *Cancer of the Breast*, The C. V. Mosby Co., 1938.
- Crossen and Crossen: *Diseases of Women*, St. Louis, 1946, The C. V. Mosby Co.
- Anderson, W. A. D.: *Synopsis of Pathology*, St. Louis, 1946, The C. V. Mosby Co.
- Blair, Moore, and Byars: *Cancer of the Face and Mouth*, St. Louis, 1941, The C. V. Mosby Co.
- Cooke, Willard E.: *Essentials of Gynecology*, Philadelphia, 1943, J. B. Lippincott Co.
- Novak, Emil: *Gynecological and Obstetrical Pathology*, Philadelphia, 1947, W. B. Saunders Co.
- Foot, N. Chandler: *Pathology in Surgery*, Philadelphia, 1945, J. B. Lippincott Co.
- Taylor and Nathanson: *Lymph Node Metastasis*, New York, 1942, Oxford University Press.
- Ackerman and del Regato: *Cancer, Diagnosis, Treatment, and Prognosis*, St. Louis, 1947, The C. V. Mosby Co.
- Warren, Shields: *Mechanism of Radiation Effects Against Malignant Tumors*, J. A. M. A. 133: 462-463 (Feb. 15), 1947.

A large amount of information relating to tumors can be obtained from the pamphlets published under the auspices of the American Society for the Control of Cancer.

CHAPTER XLVIII

DEFECTS OF BODY DEVELOPMENT

Defects of development are variously spoken of as malformations, anomalies, and monsters. The last refers to a grossly malformed fetus. Monsters are classified as *viable* (those capable of living) and *nonviable* (those not capable of living). Defects of development are due to many causes and are variously classified. Instead of entering into a prolonged discussion of the causes and the classification of the defects of development, we will discuss them as logically as possible from the standpoint of either anatomical location or physiological variation. The cause of some of these conditions has been referred to on page 455.

I. Abnormalities of Body Size

On rare occasions one sees a person who is of excessively large build or a person who is extremely small. Large builds are of endocrine origin and occur in two types, *gigantism* and *acromegaly*. Both are caused by overactivity of the anterior lobe of the pituitary gland (see page 744). Large build and obesity should not be confused.

Undergrowth, or *dwarfism*, is of two types, endocrine and nonendocrine. The endocrine types are *cretinism*, caused by a deficiency of the thyroid gland (see page 738), and *pituitary dwarfism*, caused by an inactivity of the anterior lobe of the pituitary gland (see page 745). In another endocrine type the body is small and well proportioned but the bones are childlike. This is probably caused by an interaction of several endocrine glands. The best known type of nonendocrine dwarfism is *achondroplasia*, in which the shafts of the bones fail to lengthen and the person who is otherwise of normal size has extremely short arms and legs. The condition is hereditary and is not confined to the human race as is evidenced by the dachshund.

II. The Skin and Hair

Freckles and Liver Spots.—Freckles are circumscribed areas of skin in which there is an excessive amount of skin

coloring matter (melanin). They are more common in those parts of the body exposed to light (face, neck, and back of hands). Larger areas of pigmentation occurring about the face are known as *cholasma* or "liver spots." Melanin (black substance) occurs in the deeper portion of the epidermis and is found within the cytoplasm of the cells. The depth of skin pigmentation is dependent upon the amount of melanin present.

Albinism.—Albinism is a congenital absence of coloring matter from the skin, hair, and eyes. It may be *complete* (involving the whole body) or *incomplete* (involving only a part of the body). The complete albino has a white or pink skin, white hair, and pink eyes. The pink skin is caused by the capillaries showing through the epidermis, and the lack of pigment in the retina allows the retinal vessels to show through, giving the retina a pink color. This lack of retinal coloring matter makes the eyes very sensitive to light.

In partial albinism there are irregularly sized, shaped, and distributed areas of skin from which pigment is absent. This condition is known as *leucoderma*, and persons so affected are known as "piebald" or "leopard men." The colorless areas have little tendency to enlarge. Acquired patchy loss of skin color is known as *vitiligo*.

Although albinism is more common in races with deeply colored skin, it is not unknown in the fair-skinned races. Albinism is found in practically all the domestic animals and is seen in plants. Heredity is a factor in the causation of albinism and the condition seems to run in families.

Birthmarks.—Birthmarks or vascular nevi (sing. nevus) are caused by an overgrowth and dilatation of the capillaries in the superficial layers of the corium. The color of the skin involved in a vascular nevus is not caused by a change in skin pigmentation but by the filled vessels in the corium showing through the epidermis.

Vascular nevi occur in two types, the *raised* and the *flat*. The raised type usually occurs about the face. They are present at birth or appear soon thereafter. They occur as raised, red, or bluish spongy circumscribed growths which are usually not more than a few centimeters in diameter. In some cases vascular nevi grow rapidly, but in most cases they

grow slowly to a certain point and then become stationary. They may undergo spontaneous involution. They may temporarily increase in size under such influences as crying or excitement. When occurring on the lip or ear, they cause great deformity. Vascular nevi have been referred to previously on page 553.

The flat type of vascular nevus or "port-wine stain" occurs chiefly on the face and back of the neck. These nevi are level with the skin and do not show any tendency to involve more of the skin as the child grows older. They are often unilateral in distribution and have a tendency to follow the course of the sympathetic nerves. They are smooth purplish-red or violet. Their color changes on crying, coughing, or exposure to cold.

The cause of birthmarks is not known. The theory of maternal impressions is a relic of bygone days. Vascular nevis should not be confused with pigmented nevi or pigmented moles. When the word nevus is used without qualification it usually refers to the latter, but it is often used as a more general term to designate any circumscribed congenital new growths of the skin.

Icthyosis.—This is a congenital condition in which there is dryness of the skin associated with areas of superficial thickening. This is the "fish-skinned" or "alligator" boy of the side show.

Increased Elasticity of the Skin.—The skin is attached to the body by two types of fibers, elastic and nonelastic. The nonelastic fibers restrict the distance which the skin may be pulled away from the body, while the elastic fibers pull the skin back to the body. If the nonelastic fibers grow to a great length, as occurs on rare occasions, the skin may be pulled a great distance from the body. This is the "rubber-skinned man" of the side show.

Congenital Hypertrichosis and Hypotrichosis.—Hypertrichosis is a condition in which the child is born completely or partly covered with hair. The "dog-faced boy" and the "bearded lady" are victims of congenital hypertrichosis. Localized hairy growths are often seen in the lumbar or sacral region in association with nevi. An overgrowth of the hair on the lip or other parts of the face often occurs in

women. It usually begins about the sixth year. This condition is most likely of endocrine origin. *Hypotrichosis* is a decrease in amount or complete absence of hair. With complete hypotrichosis there are usually defective nails.

III. The Face, Eyes, and Mouth

Shape of the Face.—The most common shape of the face is such that a line drawn from the eyes to the chin is straight. A few people have a concave face ("dish face"). Others have a convex face. The shape of the face is greatly influenced by the chin. The protruding chin is known as the Hapsburg chin and is characteristic of the European royal family of Hapsburg, while at least a few members of the Hohenzollern family were noted for their receding chins.

Eyes of Different Color.—This condition is rare but it does occur. It may occur in each succeeding generation or it may skip one or more generations.

Cross-Eye.—In cross-eye the axes of vision of the two eyes are not parallel, but either or both eyes may look toward its fellow (convergent cross-eye) or away from its fellow (divergent cross-eye). Both types may be found in the same family.

Nearsightedness (Myopia) and Farsightedness (Hyperopia).—The normal eyeball is practically spherical in shape. Rays of light coming from objects near the eyes are focused on the retina by the convexity of the lens becoming greater, and rays coming from faraway objects are focused on the retina by the convexity of the lens becoming less. In a nearsighted persons the eyeball is longer than in a normal person, and as the lens is unable to become flattened enough to focus the image on the retina, the image is focused in front of the retina. Biconcave glasses are used to correct this defect. In farsightedness the eyeball is so short that images of near-by objects are focused at a point behind the retina and the lens cannot become convex enough to bring the focus sufficiently forward to make the image fall on the retina. Convex lens help correct this defect. Both nearsightedness and farsightedness are inherited conditions.

Cataract.—Cataract is a clouding and opacity of the lens. It may be congenital or acquired. Heredity plays an

important part in congenital cataract. Recently it has been found that if the mother has German measles during pregnancy there is a tendency for cataract to occur in the child.

Harelip.—In its early stages (about the second month of intrauterine life) the upper jaw of the fetus consists of three parts: a central portion which bears the incisor teeth, and on each side a lateral portion which bears the “jaw” teeth. The jaw is completed by the growing forward of the lateral portions and their fusion with the central portion, while the roof of the mouth is made by two lateral bony portions coming together and fusing in the midline. If this fusion is somewhat imperfect, a cleft of the lip occurs. If the imperfection is greater, there is also a cleft in the alveolar process or the alveolar process and the palate (cleft palate).

The word harelip is a misnomer because the cleft in the lip of a hare is in the middle, while in the usual case of harelip the cleft is on one side or both sides. If it is on one side only, it is three times more common on the left side. Rarely, the cleft is in the middle; in this case it is due to a failure of fusion of the portions of the nose which form the upper lip. In rare cases there is a cleft of the palate without any change in the lip.

The cause of this condition is not known. It is more common in males than in females. Heredity seems to play a part in its origin.

Tongue-tie.—Tongue-tie is an abnormal shortness of the frenum of the tongue. This limits the movement of the tongue and brings about a characteristic type of speech. Tongue-tie is easily relieved by severing the frenum.

IV. Fistulas and Cysts of the Neck

There are two sets of fistulas and cysts in the neck: (1) branchial fistulas and cysts, and (2) thyroglossal fistulas and cysts. During embryonic life there are, on each side of the neck, structures known as branchial clefts, which in the mammals become obliterated and in fish persist to form gills. If one of these fails to be obliterated, it secretes a mucus which may be prevented from discharging and may accumulate to form a *branchial cyst*. Although the defect is present

at birth, the accumulation of fluid is not sufficient to cause a cyst to develop until later life. They are located on the side of the neck.

During early embryonic life there is a duct known as the thyroglossal duct, which extends from the thyroid gland to the posterior part of the tongue, and which later becomes obliterated. When this duct fails to become obliterated a *thyroglossal* cyst is formed. These cysts occur in the middle of the neck and are rarely present at birth but appear in infancy or young adulthood. In some cases the fistula persists without cyst formation.

V. The Breast (Mammary Gland)

The first step in the development of the breast begins about the second month of embryonic life and consists of the formation on each side of the body of a thickened ridge of epithelium which extends from the axilla to the inguinal region. This is known as the *milk line*. The line then regresses all along its course except at certain points where mammary glands will later develop. In some animals, such as the cat and dog, several of these points remain along each line. In other animals there is a single point on each line. In some cases these points are located in the pectoral region (human beings and elephants) while in others (cow and horse) they are located in the inguinal region. In the female the mammary glands begin to develop at the age of puberty; in the male they regress at puberty. One of the most common abnormalities of the mammary glands is the formation of supernumerary nipples (polythelia) or complete mammary glands (polymastia) along the milk lines. Although the supernumerary nipples and breasts usually develop along the milk lines, they may develop in locations far removed from the milk lines. As a rule, supernumerary breasts are not capable of functioning, but in some cases they are. *Amastia* is absence of breasts. It may be unilateral or bilateral. In *gynecomastia*, the male breast takes on the form of the female breast. This is probably due to an endocrine disturbance. Such breasts may secrete colostrum, but true milk secretion is rare indeed.

VI. The Extremities

Polydactylism.—By polydactylism is meant more than the normal number of fingers. The extra digit is usually a thumb or little finger. Extra fingers are often accompanied by extra toes. Webbed fingers or toes (syndactylism) is not uncommon.

Absence of Hands and Feet.—This is a rare but not unheard-of condition. A family of twelve children of which six are without hands and feet has been reported.

Absence of Arms and Legs.—Occasionally, a person is born without arms or without legs. More seldom, both arms and legs are absent. In rare cases the leg bones and arm bones fail to develop and the feet and hands are attached directly to the body, giving the appendages a resemblance to the flippers of a seal. The mermaid was probably suggested by a rare malformation in which the legs grow in a fused tapering mass, giving the body the appearance of a fish.

VII. The Internal Organs

Situs Inversus.—In this condition part or all of the organs of the body are on the side opposite to that on which they normally occur. In complete situs inversus the position of the viscera is the mirror image of the normal.

Intestinal Diverticula.—(See page 654.)

Exstrophy of the Bladder.—In some cases the abdominal wall of the fetus fails to close and with it there is a failure of closure of the anterior bladder wall, so that the bladder appears as an open gaping structure whose posterior wall may bulge forward and protrude to the outside.

Heart.—In addition to the anomalies mentioned on page 584, the heart may be absent (acardia) or project through an anterior thoracic opening which has failed to close in the process of fetal development (ectopia cordis), or it may be transposed to the opposite side of the body (dextrocardia). Dextrocardia usually occurs as a part of situs inversus.

Kidneys.—One or both kidneys may fail to develop (agnesia) or they may be small and their functional capacity greatly reduced (hypoplasia). Bilateral agnesia and hypoplasia of any great degree are incompatible with life. Unilateral agnesia and hypoplasia are rather common and usu-

ally affect the right kidney. It is most common in females. The opposite kidney is greatly hypertrophied. In some cases the two kidneys are fused at the lower poles. This is known as horseshoe kidney. In congenital cystic kidney, both kidneys are usually involved and each one is greatly enlarged and is composed of many thin-walled cysts which are filled with clear fluid or jellylike material. It is often associated with a similar condition of the liver. If extensive, this condition is not compatible with life.

Bicornate Uterus.—The vagina, uterus, and Fallopian tubes are derived by the lateral fusion of two ducts known as the ducts of Müller. In animals which give birth to a single offspring, the ducts usually fuse throughout the extent of the vagina and uterus and then remain separate to form the Fallopian tubes. In animals that have several offspring at a time, the tubes do not fuse except for a short distance above the vagina and the uterus consists of two horns (uterus bicornis). Frequently a similar lack of union occurs in women and a bicornate uterus results.

VIII. Central Nervous System

The central nervous system develops first by the formation of a groove known as the *neural groove*, along the posterior surface of the embryo. As development proceeds, the neural groove deepens and the sides fuse at the top to convert the groove into a tube within which the central nervous system develops. In some cases the groove may fail completely to become converted into a tube, but, in most cases, if there is a failure of the tube to close, the failure is partial and is located at the sacral or cranial end. When located at the cranial end, this condition is known as *cranioschisis*. When this condition is extreme and there is little development of either brain or cranial bones, there is no cranial vault and the skin passes directly from above the eyes to the occipital region, giving rise to an appearance of the head which may be described as frog-like. Fortunately these persons usually survive only a few hours.

Microcephalia is abnormal smallness of the head ("pin-head"). These unfortunates are usually imbeciles, and, if the head is extremely small, do not live long.

In *spina bifida* the neural groove fails to close at the sacral end and the laminae of the spinal column are absent. If there are no surface markings to indicate the defect, the condition is known as *spina bifida occulta*. In many cases there is a hernia of the contents of the vertebral canal beneath the skin, which may contain any or all of the following: meninges, spinal cord, or spinal fluid.

Pilonidal Sinus and Cyst.—This is a tract or cyst which may form in the midline of the body near the sacrococcygeal junction. If the external opening becomes stopped up and secretions are retained, a cyst results. The tract is lined with stratified epithelium and often contains hair. A tuft of hair may project through the external opening. There are several theories explaining the formation of pilonidal sinuses and cysts. It seems likely that they are formed from remains of the neural canal, which is attached in that area. The term pilonidal means a nest of hair.

Mongolism.—*Mongolism* or *Mongolian idiocy* is a condition in which there is a mongoloid facial appearance, deficient circulatory capacity, and lack of mentality. Mongolian idiots seldom reach a mental age of more than six or seven years, and half of them die before they are five years of age.

Hydrocephalus.—(See page 628.)

IX. Deaf-Mutism and Color Blindness

Deaf-Mutism.—Deaf-mutism is a congenital or acquired (in early childhood) defect of the organs of hearing which prevents hearing to such an extent that the power of speech cannot be acquired. A deaf-mute is often said to be “deaf and dumb.” Congenital deaf-mutism may be caused by congenital syphilis or by the mother’s having an attack of German measles during the period of gestation. Heredity also is an important factor. Deaf-mutism is extremely common in certain districts where it is associated with cretinism and goiter. A child may learn to talk and then lose his sense of hearing and become a deaf-mute as the limited speech already acquired gradually disappears. This may be prevented by cultivating the speech. The age at which deafness may cause loss of speech depends upon the intel-

ligence of the child, but, on the average, unless speech is cultivated, it will be lost if deafness occurs before the seventh year.

Color Blindness.—Color blindness is a condition in which the number of colors which may be differentiated is greatly reduced. The most common type of color blindness is an inability to distinguish between reds and greens. A less common type is an inability to distinguish between blues and yellows. In the more severe and uncommon forms, all objects appear to be some shade of gray. It is estimated that about 4 per cent of males have some degree of color blindness. It is ten times as common in males as in females. Total color blindness occurs one time in each 300,000 persons.

X. Aberrant Tissues

Tissues may be found in places other than their normal location, and these out-of-place tissues may give rise to serious disturbances. For instance, portions of endometrium (the lining of the uterus) may become implanted in the ovaries, peritoneum, umbilicus, and even in abdominal wounds. Here it undergoes menstrual changes and produces cystlike structures filled with dark blood (chocolate cysts). This condition is known as *endometriosis*. Pancreatic tissue found in the intestinal wall has been said to be a source of intestinal cancer. Aberrant thyroid tissue has been found in 10 per cent of persons and aberrant parathyroid tissue may be found in the thyroid gland.

XI. Hermaphroditism

True hermaphroditism is a rare condition in which there is present in the same person both ovarian and testicular tissue. In pseudohermaphroditism the external genitalia are so deformed that they have the appearance of the sex opposite to that indicated by the body build and other characteristics of the person.

XII. Double Monsters

Since the formation of double monsters represents the formation of identical twins gone awry, it is necessary to consider briefly the formation of twins. Twins are of two

types, *dissimilar* and *similar* or *identical*. Dissimilar twins are formed by the simultaneous fertilization of two ova. The twins may or may not be of the same sex and they have no more resemblance to each other than other siblings. Identical twins are formed from a single ovum which, in its very early stages of development, becomes divided into two parts, with each part developing into a child. Such twins are of the same sex and closely resemble each other in physical and mental characteristics. Triplets, quadruplets, and quintuplets may be dissimilar or identical or combinations of the two. For instance, triplets may arise from one, two, or three ova. If they arose from two ova, there would be two identical twins plus one dissimilar child.

If a fertilized ovum commences to develop and then begins to divide into two parts, but the separation is incomplete, a *double monster* instead of identical twins results. Double monsters may be classified as (1) equal conjoined twins and (2) conjoined twins in which one is smaller than the other. Equal conjoined twins may be joined at the head, chest, or in the lower pelvic region. These combinations give various types of deformity, such as (a) two well-formed bodies not extensively joined (Siamese twins) (b) one body, one set of limbs, and two heads, (3) one head, two arms, four legs, etc., and myriads of other types.

If something happens to interfere with the development of one of the twins and it does not develop, this one becomes attached to the larger one as a *parasitic fetus*. Fortunately, most double monsters except the equally but not extensively joined twins do not survive for any length of time.

Questions for Review

1. What is meant by microcephalia?
2. Characterize an extreme case of cranioschisis found in a defective central nervous system.
3. Discuss, briefly, the conditions and occurrences of color blindness.
4. With regard to body size, give the causes and effects of pituitary dwarfism and cretinism.
5. Give the term applied to cases in which an individual's eyeball is longer than normal and the lens is unable to become flattened enough to focus the image on the retina. What correction for this defect is recommended?

6. What may result if one of the branchial clefts is not obliterated? Are these clefts present during the embryonic period of growth?
7. Give the characteristics of one disturbance caused by the occurrence of aberrant tissue in the body.
8. What is meant by the term hermaphroditism?
9. What term is applied to the absence of breasts? What forms does it take?
10. Characterize mongolism.

True-False Test

- 1. The appearance of the white or pink skin of an albino is due to the lack of melanin in the epidermal layer of the skin.
- 2. With regard to abnormalities of body size, the large build of an individual is correlated with obesity.
- 3. The vascular nevi, caused by an overgrowth and dilatation of the capillaries in the superficial portions of the skin, are characterized by a change in skin pigmentation.
- 4. Cross-eye is characterized by axes of vision in the two eyes which do not parallel, and either or both eyes may look toward its fellow or away from its fellow.
- 5. The term "harelip" is appropriately assigned to cases of imperfect fusion of the bony portions of the midline of the roof of the mouth.
- 6. Syndactylism is the occurrence of webbed fingers or toes and is not uncommon.
- 7. In congenital cystic kidney, both kidneys are usually involved and each is greatly enlarged and is composed of many thin-walled cysts which are filled with clear fluid or jellylike material.
- 8. Deaf-mutism is determined through the genetic background of the patient and should not be correlated to environmental causes whatsoever.
- 9. Double monsters may be classified as (1) equally conjoined twins and (2) conjoined twins in which one is smaller than the other. Equally conjoined twins may be joined at the chest, head, or in the lower pelvic region.

Completion Test

1. Gigantism and acromegaly are caused by an overactivity of the ----- lobe of the ----- gland.
2. Large areas of pigmentation occurring about the face are known as ----- or "liver spots."
3. Both myopia and hyperopia are acquired through ----- conditions.
4. The milk line consists of a thickened ridge of epithelium which extends from the ----- to the inguinal region.

5. In gynecomastia, the ----- breast takes the form of the ----- breast.
6. The absence of a heart is known as -----.
7. The vagina, uterus, and Fallopian tubes are derived by the lateral fusion of two ducts known as the -----.
8. A congenital condition known as ----- is characterized by an extreme dryness of skin associated with areas of superficial thickening.
9. Birthmarks are known as -----.
10. ----- is a condition in which a child is born completely or partly covered with hair, while ----- is indicative of the abnormal decrease or complete absence of hair.

References

- Karsner, Howard L.: Human Pathology, Philadelphia, 1942, J. B. Lippincott Co.
- Boyd, William: Textbook of Pathology, Philadelphia, 1947, Lea & Febiger.
- Patton, Bradley M.: Human Embryology, Philadelphia, 1946, The Blakiston Co.
- Lewis, J. H.: Biology of the Negro, Chicago, 1942, The University of Chicago Press.
- Murphy, Douglas P.: Congenital Malformations, 1940, Philadelphia, University of Pennsylvania Press.
- Whitney, David D.: Family Skeletons, Lincoln, 1946, University of Nebraska Press.
- Gruenwald, Peter: Mechanisms of Abnormal Development, Arch. Path. 44: 398 (October), 1947.

CHAPTER XLIX

DISEASES OF THE HEART AND BLOOD VESSELS

I. THE HEART

Diseases of the heart have been classified in many ways. One classification, which has the advantage of indicating the etiology of the condition being discussed, divides heart diseases into congenital, rheumatic, syphilitic, and hypertensive (caused by high blood pressure).

A. Congenital Defects

Congenital diseases of the heart may be brought about by defects in the germ plasm which interfere with the orderly development of the heart, defective nutrition through the placenta, syphilis, or bacterial infections. Slight defects may not have any effect on the heart other than making it more susceptible to bacterial infection, but extensive defects may seriously impair the capacity of the heart to perform its work or may render postnatal life impossible.

Various defects of the cardiac septa may occur. Defects in the intra-auricular or intra-ventricular septa, if large enough, allow venous blood to be shunted from the right to the left side of the heart. The presence of venous blood in the arteries produces cyanosis, and infants so affected are known as "blue babies." This condition is most often due to a failure of closure at birth of the foramen ovale.

The imperfect circulation accompanying congenital heart disease causes proliferative changes in the tissues, prominent among which are thickening of the lips and nose and clubbing of the ends of the fingers. Congenital heart diseases are of special danger because of the predisposition to subacute bacterial endocarditis which they bring about.

B. Hypertrophy and Dilatation of the Heart

Hypertrophy.—By hypertrophy of the heart is meant an increase in the amount and strength of the heart muscle in

response to an increase in the amount of work thrown upon it. The most important causes of hypertrophy are: (1) obstruction to the flow of blood through the vessels, (2) conditions within the heart itself, and (3) pericardial adhesions. Seldom does hypertrophy affect all the cavities of the heart equally, the cavity or cavities chiefly affected depending on the cause of the hypertrophy. Because of their thin muscular walls the atria are much less capable of undergoing hypertrophy than the ventricles.

When there is an increased resistance to the flow of blood through the systemic vessels, the left ventricle undergoes hypertrophy; when there is an increased resistance in the pulmonary circulation as occurs in emphysema or pulmonary congestion brought about by valvular disease of the heart, the right ventricle undergoes hypertrophy. In certain cases of pericardial adhesion hypertrophy occurs because the musculature of the heart is forced to pull the surrounding parts inward during systole or push them outward during diastole.

There is a limit to the hypertrophy which the heart may undergo, and when this limit is passed dilatation occurs and the heart is left in a worse condition than before.

Dilatation of the Heart.—Dilatation of the heart is of two types: passive and active. Passive dilatation occurs without weakening of the heart muscle or thinning of the cavity wall for the purpose of holding an increased amount of blood when it becomes necessary for a cavity to expel more blood than normal. It may be temporary, as occurs in severe exercise when each contraction of the left ventricle is sending an increased amount of blood to the systemic vessels and each contraction of the right ventricle is sending an increased amount to the lungs, or it may be permanent as occurs in certain valvular diseases of the heart.

In active dilatation the affected cavity dilates widely and its wall becomes thin because the muscle fibers have, to a great extent, lost their ability to contract. It may occur suddenly, as when one engaging in strenuous exercise drops dead. It may also occur in certain infectious diseases, disease of the

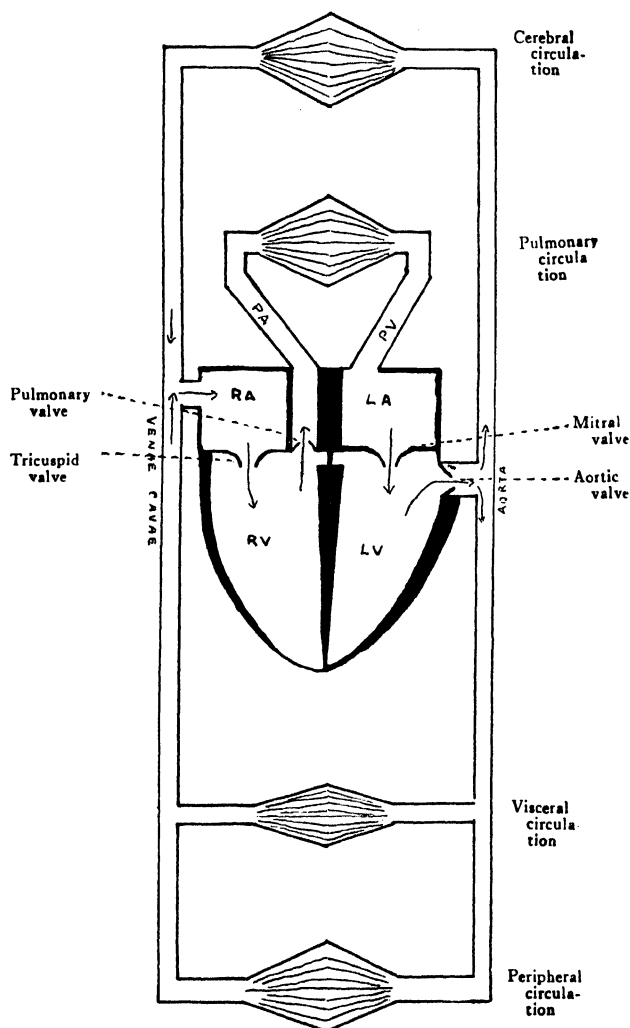


Fig. 156.—A schematic representation of the general circulation of the body. The blood leaves the left ventricle (LV) and enters the aorta through which it passes to the visceral and peripheral vessels to supply the abdominal organs and the limbs. From the aorta it passes through the carotids and vertebrals to supply the brain. After passing through the various organs, it is returned to the heart, which it enters through the right auricle (RA). From there it passes to the right ventricle (RV), from which it is carried to the lungs by the pulmonary artery (PA); it then reaches the left auricle (LA) through the pulmonary vein (PV). The pulmonary vein carries arterial blood. If the mitral valve is so affected by disease that it is no longer able to prevent the blood from being forced back into the left auricle during ventricular systole (insufficiency), at every beat of the heart some of the blood which should be sent into the aorta is pushed back into the auricle and

coronary arteries, and when a hypertrophied heart fails. Due to toxic action and increased pulmonary resistance, active dilatation of the right ventricle may occur in pneumonia.

C. Endocarditis

Endocarditis is inflammation of the endocardium. It is one of the most common diseases of the heart and is of importance on account of both its immediate effects and the permanent injury which it produces. As a rule, the process is confined to the endocardium of one or more valves, but it may extend to the endocardium of the cavity wall. The word "endocarditis" without qualification means valvular endocarditis. When the endocardium of the wall of the heart is affected, it is spoken of as "mural" endocarditis. In adults, the valves of the left side of the heart are most often affected and the mitral valve is affected more often than the aortic. In fetal life those of the right side of the heart are most frequently involved. In some cases only one valve is affected; in others, more are involved.

When bacteria are deposited on a valve, they injure the covering endothelium and cause the valve to become swollen. Fibrin, platelets, and blood cells are deposited on the injured endothelium, and thrombi are formed. These thrombi are known as *vegetations*. In severe cases necrosis may occur and lead to ulceration or complete destruction of one or more cusps of the valve. Vegetations or ulcerations alone or with their reparative changes, characterized by thickening, retraction, and adhesion of the cusps of the valve, or the destruction of one or more cusps of a valve, bring about changes which lead to incomplete closure of the valve. The passage of blood through the incompletely closed orifice causes abnormal blowing sounds known as "murmurs."

Partly from the standpoint of effect produced and partly from the standpoint of etiology, endocarditis may be classi-

eventually into the lungs. The lungs become the seat of a "passive congestion." Eventually the back pressure affects the right side of the heart also so that the right chambers become dilated, and after a time the tricuspid valve becomes unable to prevent reflux of blood (insufficiency). Then, of course, the liver and other viscera will become passively congested. (From Woolley: *Fundamentals of Pathology*, The C. V. Mosby Co.)

fied as: (1) acute, simple, or vegetative endocarditis in which there is little tendency for the vegetations to ulcerate; (2) acute ulcerative endocarditis in which ulceration and destruction of tissue are distinguishing features; (3) subacute bacterial endocarditis which is characterized by moderate ulceration and a slow course; and (4) chronic endocarditis which from the standpoint of pathology is almost synonymous with chronic valvular disease. Acute endocarditis is most often caused by *Streptococcus hemolyticus*, and subacute bacterial endocarditis is most often caused by *Streptococcus viridans*.



Fig. 157.—Clubbing of the fingers in a case of subacute bacterial endocarditis. Clubbing of the fingers accompanies many chronic diseases of the heart and lungs. (From Meakins: *The Practice of Medicine*. The C. V. Mosby Co.)

As a rule, in neither acute endocarditis nor subacute bacterial endocarditis do vegetations on the valves of the heart interfere with its action. Subacute bacterial endocarditis is characterized by its uniformly fatal termination. Many cases of subacute bacterial endocarditis give a history of preceding dental extractions.

D. Valvular Defects of the Heart

Valvular defects are of two types. In one type the cusps of the valve become shortened, thickened, curled or otherwise

deformed, so that the valve cannot close properly and the blood leaks back into the cavity behind the lesion when the cavity in front of it contracts. For instance, when the mitral valve is so affected, blood leaks back into the left atrium during contraction of the left ventricle. This type of lesion is called an *insufficiency* or *incompetency* of the valve or, from the standpoint of blood flow, a *regurgitation*. In *stenosis*, the second type of defect, the orifice becomes narrow on account of contraction of the supporting ring, the projection of stiffened cusps, or adhesions between the edges of the cusps. Insufficiency and stenosis are frequently associated.

Valvular defects are usually a result of the destruction of tissue with scar formation brought about by an endocarditis, but syphilis is not infrequently a cause of chronic valvular disease. The aortic valve is most often affected by syphilis, and the process usually represents an extension of a syphilitic involvement of the aorta.

Since it is usually an aftermath of endocarditis, chronic valvular disease arising during adult life will most often affect the mitral or aortic valve, while the right side of the heart is most often affected when the disease arises during fetal life.

When a valve becomes stenosed, the cavity forcing the blood through the valve undergoes hypertrophy in order to overcome the obstruction to the blood flow. In regurgitation the cavity behind the affected valve and the one in front of it undergo hypertrophy and passive dilatation in order to take care of the normal amount of blood plus that which is regurgitated. As has been said there is a limit to cardiac hypertrophy, and when the limit is passed the muscle gives way and active dilatation follows. The atria suffer active dilatation much more quickly than the ventricles when an extra burden is thrown upon them. As long as the hypertrophied heart furnishes sufficient blood to the body, the defect is said to be *compensated*, and when failure occurs it is said to be *decompensated*. Decompensation is characterized by dyspnea, edema, cyanosis, ascites, and enlargement of the liver.

E. Coronary Disease

By coronary disease is meant disease of the coronary arteries. These arteries supply nourishment to the musculature of the heart. Coronary disease is of importance because the most common cause of sudden death is heart failure and the most common cause of heart failure is the cutting off of the blood supply of a portion of the heart wall by an occlusion of one of the larger branches of the coronary arteries. This is the cause of 40 per cent of sudden and unexpected deaths. Occlusion may occur suddenly or gradually. In the latter case the artery becomes narrower and narrower until at last it is unable to supply the portion of the heart muscle that is dependent upon it with sufficient blood and the muscle dies; this brings about heart failure. Occlusion seldom occurs in a coronary artery that is not diseased.

Coronary occlusion may occur as a result of (1) arteriosclerosis and narrowing, (2) thrombosis of an already arteriosclerotic artery, (3) syphilitic involvement of the mouths of the coronaries and (4) blocking of the vessel by an embolus. The victim of a coronary occlusion may die instantly (the most common result), die after a few days, or recover. The disease is specially common among doctors and professional men. So common is it among doctors that it has been called the "disease of doctors."

II. THE BLOOD VESSELS

A. The Arteries

Arteriosclerosis.—This term indicates an inflexibility and hardening of the arteries brought about by various combinations of degeneration, formation of scar tissue, and deposit of calcium salts. In some cases calcification may be so extensive that the vessel crackles between the fingers when crushed. Arteriosclerosis has been attributed to various causes, such as alcoholism, overeating, syphilis, gout, and Bright's disease, but we are yet in ignorance of its exact cause. The process is generalized in some cases while in others it is localized, as in arteriosclerosis of the renal or cerebral vessels.

Aneurysm.—An *aneurysm* is a localized dilatation of the arterial wall most often brought about by the combined effects of weakening of the vessel wall and high blood pressure. The most common types are fusiform in which there is a spindle-shaped dilatation of the whole circumference of the artery and saccular in which there is a saclike dilatation, due to weakening of a limited area of the wall.

Aneurysms usually occur after the forty-fifth year. On account of its destructive effect on the vascular walls and its frequency, syphilis is the most important single factor in the production of aneurysms.

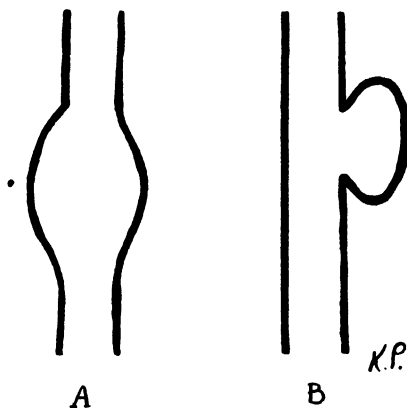


Fig. 158.—Types of aneurysm. A, fusiform; B, saccular.

Aneurysms develop slowly and may reach a diameter of three or four inches. The blood often clots within the sac, and this furnishes some protection to its thin, weak wall. As the sac enlarges, the surrounding tissues are eroded or pushed aside. It is not uncommon for an aneurysm of the ascending arch of the aorta to erode the ribs and sternum and appear beneath the skin as a pulsating mass. Aneurysms ultimately rupture, and in the case of the larger ones the rupture causes sudden death. The rupture of saccular aneurysms of the cerebral arteries is one of the causes of cerebral hemorrhage (apoplexy). Superficial aneurysms have been mistaken for abscesses and opened, with disastrous results.

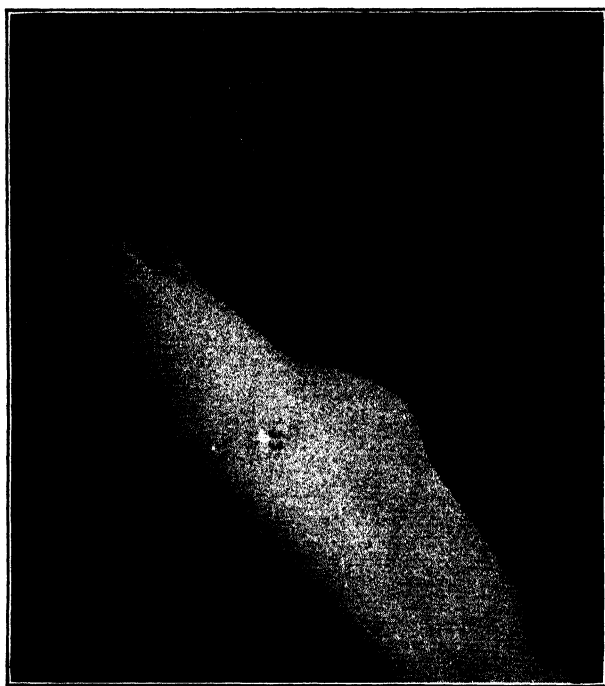


Fig. 159.—Bulging of the chest due to an aneurysm of the ascending arch of the aorta. (From Meakins: *The Practice of Medicine*.)

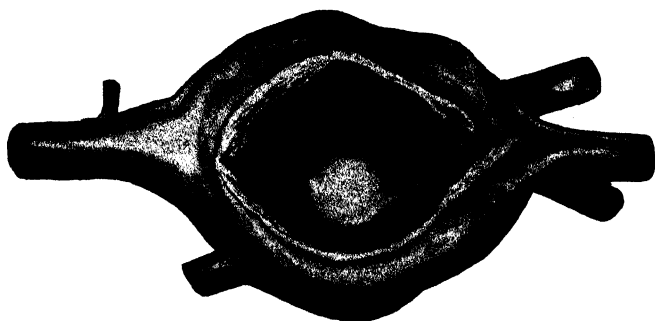


Fig. 160.—Aneurysm of popliteal artery. (From Karsner: *Human Pathology*. J. B. Lippincott Co.)

B. The Veins

Varicose Veins (Varix).—When the amount of blood which the veins have to support is increased by some interference with the return of venous blood to the heart and their walls become weakened, they dilate and become tortuous. This is probably due to the lack of muscle fibers in the venous wall, and on account of the action of gravity the condition is more pronounced in the lower extremities. Causes which may produce an obstruction of the venous return and predispose to varix formation are poor heart action, overwork, long standing, pregnancy, and abdominal tumors. Loss of support by the surrounding tissues as occurs in generalized weakness may be a contributing cause.

The most frequent site of varicose veins is the inside of the leg. Other types of varix are esophageal varix, varicocele (varix of the spermatic cord), and hemorrhoids (varix of the anal veins).

Varicose veins are especially liable to mechanical injury, inflammation, and hemorrhage. The tissues drained by varicose veins are extremely liable to infection and heal poorly.

Questions for Review

1. Classify heart diseases according to their etiology.
2. Why are "blue babies" so called?
3. What tissue changes may occur as a result of imperfect circulation accompanying congenital heart disease.
4. Name the most important causes of hypertrophy of the heart.
5. What is meant by dilatation of the heart? What are the two kinds of dilatation?
6. What changes occur in the heart as a result of endocarditis? How may endocarditis be classified?
7. What is stenosis? What is regurgitation?
8. How does the heart react to stenosis or insufficiency of one of its valves?
9. What is meant by compensation? What is decompensation?
10. What are the causes of coronary occlusion?
11. Describe the changes which take place in the arterial wall in arteriosclerosis?
12. What is an aneurysm? Where do aneurysms most commonly occur?
13. What are varicose veins? What are some predisposing causes of varicose veins?

True-False Test

- 1. Normally the foramen ovale should not close at birth.
- 2. Hypertrophy usually affects all cavities of the heart equally.
- 3. When a compensating heart can no longer meet the demands placed upon it, it dilates and decompensation begins.
- 4. When the total amount of blood in the chambers of the heart is greatly increased, dilatation of the heart may occur.
- 5. Endocarditis is usually of bacterial origin and involves the valves of the heart.
- 6. Endocarditis is often associated with acute rheumatic fever, chorea, and tonsillitis.
- 7. "Mural" endocarditis is an inflammation of the wall of the heart.
- 8. Subacute bacterial endocarditis is always fatal in its termination.
- 9. Victims of coronary occlusion never recover.
- 10. Forty per cent of sudden deaths result from coronary occlusion.
- 11. A saccular aneurysm involves the whole circumference of the artery.
- 12. The most common cause of aneurysm is syphilis.

Completion Test

- 1. In fetal endocarditis, the ----- valve is more often affected than is the ----- valve.
- 2. In endocarditis of adults the valves of the ----- side of the heart are more often affected.
- 3. When bacteria are deposited on a valve, thrombi, known as -----, are formed.
- 4. Stenosis of a valve results in ----- of the cavity forcing blood through the valve.
- 5. So common is it among doctors that ----- is called the "disease of doctors."

References

- Wiggers, Carl J.: *Physiology in Health and in Diseases*, Philadelphia, 1944, Lea & Febiger.
- Boyd, William: *A Textbook of Pathology*, Philadelphia, 1947, Lea & Febiger.
- Karsner, Howard T.: *Human Pathology*, Philadelphia, 1942, J. B. Lippincott Co.
- White, Paul D.: *Heart Diseases*, New York, 1944, The Macmillan Co.
- Moore, R. A.: *Textbook of Pathology*, Philadelphia, 1944, W. B. Saunders Co.

CHAPTER L

THE BLOOD AND ITS DISEASES

The blood consists of an aqueous solution of proteins and salts, known as plasma, in which are suspended erythrocytes (red blood cells), leucocytes (white blood cells), and platelets. The function of the erythrocytes is to transfer oxygen to the body cells. This property resides in hemoglobin, the



Fig. 161.—Taking blood from the finger of a child. The blood is taken in a special diluting pipette and will later be placed on a counting chamber and the cells counted under the microscope. Dilutions for red and white cells are made in different pipettes and with different diluting fluids.

iron-bearing pigment of the cell. The leucocytes aid in intestinal absorption and destroy bacteria and other foreign materials by phagocytosis, and the platelets play a part in the coagulation of blood. The plasma gathers and trans-

ports food material to the body cells and conveys their waste products to the kidneys, lungs, intestines, and skin to be excreted.

I. RED BLOOD CELLS AND HEMOGLOBIN

Throughout life red blood cells (erythrocytes) are constantly being produced and destroyed. In the latter months of fetal life they are produced by the liver and spleen. After birth this function is transferred to the bone marrow, and the marrow of practically all bones takes a part in the process. When adult life is reached the process is limited to the marrow of the ribs, sternum, and vertebrae; and the red cells that have outlived their period of usefulness are destroyed by the phagocytic cells of the reticuloendothelial system, particularly those of the spleen, and their hemoglobin is converted into bile pigment. When there is an extreme demand for erythrocytes, as may happen as a result of excessive destruction or failure of normal production, the marrow of bones ordinarily not concerned in erythrocyte production may assume that activity, and the liver and spleen may attempt again to discharge their embryonic erythrocyte-producing functions.

Under normal conditions erythrocyte production and destruction are so evenly balanced that a level of 4,500,000 to 5,000,000 cells per c. mm. of blood is constantly maintained. Stained smears of the blood will show all the red cells to be alike. These cells are known as normocytes. When for some reason red cell destruction is greatly increased, or the bone marrow becomes incapable of producing the required number of mature cells, immature cells, such as reticulocytes (cells showing a skein in their cytoplasm), polychromatophils (deeply staining cells), and normoblasts (nucleated red blood cells) appear in the blood stream, showing that the bone marrow is attempting to compensate for its failure to furnish the required number of mature cells by substituting immature forms.

The hemoglobin content of the blood is usually expressed in percentage of normal. The normal hemoglobin content of the blood is about 16 grams per 100 c.c. The color index is

an expression of the hemoglobin content of the individual cell in relation to normal. It is calculated by dividing the percentage of hemoglobin by the percentage of red blood cells, taking 5,000,000 cells per c. mm. to represent 100 per cent. For instance, a person with 3,000,000 red cells and 45 per cent of hemoglobin would have a color index of 0.75. The normal color index is about 1.

Anemia

Anemia is an impoverishment of the blood due to a decrease in red cells, hemoglobin, or both. In most instances both red cells and hemoglobin are decreased but not in the same proportion so that in one case the color index may be low while in another case it may be high.

From the clinical standpoint anemia may be classified into two types: primary and secondary. A secondary anemia is one whose cause is obvious (example—hemorrhage), while in a primary anemia no cause is obvious, and it is assumed that the anemia is due to a derangement of the hematopoietic system.

A classification based on etiology is that of Ottenberg. This classification, with many subheads deleted, is as follows:

I. Deficiencies

- A. Iron deficiencies (ex. loss of blood, hookworm, etc.)
- B. Deficiency in “antianemic principle” (ex. pernicious anemia)
- C. Nutritional deficiencies (ex. anemia of vitamin deficiencies)

II. Injury to the Blood-Making Organs

- A. Toxic destruction of bone marrow (ex. action of x-ray on marrow)
- B. Mechanical replacement of marrow (ex. tumor growth of marrow)
- C. Interference with regeneration of blood of some intermediate stage (ex. certain diseases of spleen and liver)

III. Disintegration of Blood (Hemolysis)

- A. Caused by hereditary defects of red cells themselves (ex. hemolytic icterus, sickle cell anemia)
- B. Toxic destruction of blood (ex. infections, intestinal parasites, hemolytic poisons)

Another classification is based on the size of the red blood cells and their hemoglobin content. This is not an etiological classification but it has a decided advantage in that by following the hematological procedures on which it is based the anemias are often correctly diagnosed and a definite mode of therapy is often suggested. When this classification is used, the anemias are divided primarily into *macrocytic*, *normocytic* and *microcytic* depending on whether the erythrocytes are larger than normal, of normal size, or smaller than normal and are divided secondarily into *hyperchromic*, *normochromic* and *hypochromic* depending on whether the cell contains more hemoglobin than normal, a normal amount, or less than normal. Using this classification we have the following types of anemia:

1. *Macrocytic-hyperchromic* (the red blood cells are larger than normal and contain more hemoglobin than normal).
2. *Macrocytic-normochromic* (the red blood cells are larger than normal but contain only the normal amount of hemoglobin).
3. *Macrocytic-hypochromic* (the red blood cells are larger than normal but contain less than the normal amount of hemoglobin).
4. *Normocytic-normochromic* (the cells are of normal size and contain a normal amount of hemoglobin).
5. *Normocytic-hypochromic* (the red blood cells are of normal size but contain less than the normal amount of hemoglobin).
6. *Microcytic-hypochromic* (the red blood cells are both smaller than normal and contain less than the normal amount of hemoglobin).

Secondary Anemia.—Among the various causes of secondary anemia are acute and chronic hemorrhage. Immediately after an acute hemorrhage the cell count of the blood is un-

affected because all the constituents of the blood have been lost in their normal proportions. After a few hours Nature begins to make up for the loss in volume by transferring fluids from the tissues to the blood vessels, and the cell count begins to fall but the color index remains unchanged because the relation existing between red cells and hemoglobin is not disturbed. At a later period, regeneration begins with a more rapid replacement of red cells than hemoglobin, which causes the color index to fall below normal.

Other causes of secondary anemia are such wasting diseases as cancer, tuberculosis, pellagra, and sprue. A secondary anemia is frequently associated with rickets, intestinal parasites, septicemia, malaria, and syphilis. The anemia of syphilis is often aggravated by antiluetic treatment. Contact with certain chemicals, such as lead, mercury, arsenic, and benzene, or the taking of acetanilid, an important constituent of many patent headache remedies, may lead to a profound secondary anemia. In some cases of extreme secondary anemia the red cells may fall below 1,000,000 per c. mm., and the hemoglobin may fall to 20 per cent giving a blood picture closely resembling pernicious anemia. One important differential point is that in these cases, as is the case in practically all secondary anemias, a leucocytosis is present, while in pernicious anemia a leucopenia (decrease in white blood cells) is the rule. The air hunger that often accompanies anemia is caused by the amount of hemoglobin being reduced to such an extent that it is incapable of transporting enough oxygen to meet the demands of the tissues.

The Primary Anemias.—The most important primary anemias are pernicious anemia, chlorosis, and aplastic anemia. Sickie-cell anemia and the anemia of pregnancy will be considered with this group since their true nature is not definitely known.

Pernicious anemia is characterized by remissions and exacerbations and, untreated, always ends in death. It seems to be caused by a lack of something which is essential to the building of the stroma of red blood cells rather than to some primary disorder of the erythrocyte-producing tissues. The provision of this stroma-building substance by the feeding of

liver or desiccated stomach forms one of the most brilliant chapters of modern therapeutics. Pernicious anemia is characterized by its peculiar blood picture, the absence of free hydrochloric acid from the stomach, a lemon yellow color of the skin, and a well-nourished appearance.

The red blood cells are often reduced to 1,000,000 per c. mm. or less, but the hemoglobin is not reduced in proportion, which gives a color index of more than 1. As a whole the cells are larger than normal. This combination of cells larger than normal and a color index of more than one classifies pernicious anemia as a macrocytic hyperchromic anemia. So frequently does the absence of free hydrochloric acid from the stomach accompany pernicious anemia that most hematologists refuse to make a diagnosis of pernicious anemia when hydrochloric acid is present. A smooth, red, painful tongue, and cord changes leading to neurological disturbances are frequently present.

Chlorosis is an anemia, affecting females about the time of puberty, that is characterized by a marked reduction in hemoglobin without a proportionate reduction in erythrocytes which gives a color index less than 1. Characteristics of the disease are the peculiar blood picture, marked pallor, a green hue of the skin, shortness of breath, and constipation. The disease is comparatively common in Europe but is infrequent in America.

Aplastic anemia is a rare disease in which the erythrocyte-producing activity of the bone marrow ceases, and the natural destruction of the red cells quickly leads to a fatal anemia. Why the bone marrow ceases to manufacture cells is not known. The blood shows no abnormality other than a great reduction in red and white cells and in hemoglobin. A bone marrow inactivity of greater or less degree may also be caused by certain drugs, notably benzol and arsphenamine. Aplastic anemia is a normocytic normochromic anemia.

Anemia is often associated with the latter months of pregnancy, or it may make its appearance from six to eight weeks after delivery and prove fatal within four to six weeks. As a rule, labor is short, painless, and free from bleeding. Second attacks are not common.

Sickle-cell anemia is a peculiar type of anemia in which a large proportion of the red blood cells have a crescentic shape. It is an hereditary disease and apparently is confined to the Negro race.

Erythroblastosis fetalis attacks the fetus before it is born or within the first few days of postnatal life. It is characterized by destruction of erythrocytes and a great increase in nucleated red blood cells (erythroblastosis). Other signs which may be present are edema, jaundice, pallor, and enlargement of the liver and spleen. The occurrence of erythroblastosis fetalis may be explained by a consideration of the following facts: When a guinea pig is given repeated injections of the red blood cells of a Rhesus monkey, the serum of the guinea pig will acquire the ability to agglutinate the red cells of Rhesus monkeys. Also it will agglutinate the red blood cells of a large majority of human beings (85 per cent of the Caucasian race; more in others). The red blood cells which are agglutinated are said to contain the Rh factor and the person from which the cells were removed is said to be *Rh positive*. Persons who do not have the Rh factor in their red blood cells are said to be *Rh negative*. If an Rh-negative mother and Rh-positive father have children, at least part of the children will be Rh positive. In rare cases, due to placental defects, the Rh-positive cells of the fetus get into the blood stream of the mother and the blood of the mother develops antibodies against the Rh factor. The antibodies against the Rh factor then get through the placenta and attack the red blood cells of the fetus and destroy them. Erythroblastosis seldom occurs during the first pregnancy, but when it once makes its appearance there will be a repetition of the condition in about 80 per cent of subsequent pregnancies. The transfusion of an Rh-negative person with the blood of an Rh-positive person may lead to serious post-transfusion reactions.

Depending on the symptoms and signs which predominate, the disease occurs in three clinical forms: hydrops fetalis, icterus gravis neonatorum, and congenital anemia of the newborn. In *hydrops fetalis* or universal edema, which is characterized by extreme edema, the child is born dead or dies within a few hours. In *icterus gravis neonatorum*, which is

characterized by jaundice at birth or appearing soon thereafter, death usually does not occur until the first or second week of extrauterine life. About one-fourth of these patients recover. *Congenital anemia of the newborn* is the least severe of the three conditions. There is usually a rather profound anemia without jaundice or edema.

II. LEUCOCYTES

Unlike the red blood cells which in their mature stage are of a single type, there are several varieties of leucocytes which differ in their origin, appearance, and function. The following are the leucocytes, with their percentage, encountered in normal blood.

Polymorphonuclear Leucocytes	60-70 per cent
Large Lymphocytes	5-10 per cent
Small Lymphocytes	20-25 per cent
Large Mononuclears	} 2- 6 per cent
Transitionals	
Eosinophiles	1- 4 per cent
Basophiles	$\frac{1}{2}$ - 1 per cent

The polymorphonuclear leucocytes, eosinophiles, and basophiles are known as *granulocytes* on account of the granules in their cytoplasm. The other leucocytes do not contain granules in their cytoplasm and are known as *hyaline* leucocytes. The granulocytes are formed in the bone marrow. The lymphocytes are formed in the lymph nodes and other lymphoid tissues. Leucocytes are destroyed by passing through the wall of the intestines to the feces and through the bronchial wall to the bronchial secretions.

As a result of disease the normal percentage relation existing among the different types of leucocytes is profoundly disturbed. The determination of this percentage is known as a *differential count*.

A. Leucocytosis

Normally the number of leucocytes ranges from 5,000 to 8,000 per c. mm. of blood. As a result of disease the number may be increased or decreased. A more or less transient increase in number brought about for the purpose of com-

bating some injurious agent is known as a *leucocytosis*. A more permanent, and in most cases a greater, increase due to disease of the leucocyte-producing tissues themselves, is known as *leucemia*. Leucocytosis is a protective mechanism while leucemia is a destructive process with more than a superficial resemblance to a malignant tumor.

When a leucocytosis occurs there is not a proportional increase in all types of leucocytes, but as a rule only one or two types are affected.

In *polymorphonuclear leucocytosis* total counts of 20,000 to 30,000 per c. mm. are frequent; more than 50,000 is not uncommon but 100,000 is seldom exceeded. With counts such as these from 85 to 95 per cent of the total leucocytes are polymorphonuclears. A polymorphonuclear leucocytosis is most often associated with acute suppurative conditions, such as acute appendicitis, salpingitis, peritonitis, and meningitis. Septicemia and certain acute infectious diseases, such as pneumonia, acute rheumatic fever, erysipelas and smallpox, also are accompanied by a polymorphonuclear leucocytosis. When conditions which usually cause a polymorphonuclear leucocytosis fail to do so, a very mild infection or failure on the part of the body to react is indicated. The latter is of grave significance.

Certain common diseases show either no change in the number of leucocytes or a *leucopenia* (decrease in the number of leucocytes). The most important of these are typhoid fever, tuberculosis, measles, German measles, mumps, and influenza. They may, however, be complicated by conditions that cause a leucocytosis, as is the case when perforation or hemorrhage complicates typhoid fever. *Agranulocytic angina* is characterized by ulceration of the mouth and throat and a marked reduction in the polymorphonuclear leucocytes. Counts from typical cases may show the total leucocytes to be reduced to less than 1,000 and the percentage of polymorphonuclear cells to less than ten. The prognosis is very grave.

A *lymphocytosis* (increase in the number of lymphocytes) accompanies typhoid fever, whooping cough, Malta fever, and syphilis. It should be remembered that a lymphocytosis may

PLATE XVI.—BLOOD CELLS—GIEMSA STAIN

Scale 1 mm. = 1 micron.

- | | |
|---|---|
| 1.* Myeloblast (progenitor of cells 2 to 13 inclusive). | 25.* Plasma cell. |
| 2.* Promyelocyte. | 26.* Irritation cell. |
| 3,* 4,* 5,* 6.* Myelocytes. | 27,* 28,* 29,* 30,* 31.* Nucleated red blood cells. |
| 7, 8, 9, 10. Young polymorphonuclear leucocytes. | 32,* 33.* Very large red blood cells. |
| 11. Mature polymorphonuclear leucocyte. | 34. Normal red blood cell (Normocyte). |
| 12. Eosinophile. | 35.* Very small red blood cell. |
| 13. Basophile. | 36.* Red blood cell with dividing nucleus. |
| 14.* Lymphoblast (progenitor of cells 15 and 16). | 37.* Faintly polychromatic erythrocyte. |
| 15. Large lymphocyte. | 38.* Polychromatic erythrocyte. |
| 16. Small lymphocyte. | 39.* Basophilic punctation, fine. |
| 17.* Reticuloendothelial cell. | 40.* Basophilic punctation, coarse. |
| 18. Transitional. | 41.* Poikilocytes. |
| 19, 20. Mononuclears. | 42.* Marginal granule. |
| 21.* Endothelial element. | 43.* Malaria parasite. |
| 22.* Atypical promyelocyte. | 44,* 45.* Cabot's ring bodies. |
| 23.* Micromyeloblast. | 46. Red blood cell with lack of color. |
| 24. "Twin-nuclear" cell of Schilling. | 47.* Hyperchromatic erythrocyte. |
| | 48. Blood platelets. |

(From Gradwohl, *Clinical Laboratory Methods and Diagnosis*, The C. V. Mosby Co., St. Louis)

occur without an increase in the total number of leucocytes, because the polymorphonuclear leucocytes may be reduced at the same time. The presence of a high leucocyte count (20,000 to 30,000) and a marked increase in lymphocytes (50 to 70 per cent) is alone very suggestive of whooping cough.

An *eosinophilia* (an increase in eosinophiles above 5 per cent) occurs in malaria, asthma, certain skin diseases, scarlet fever, and myeloid leucemia. It is also a frequent accompaniment of infestations with certain intestinal parasites, particularly hookworms and tapeworms.

The *large mononuclear and transitional leucocytes* are increased in typhoid fever, malaria, and amebic dysentery.

An increase in *basophiles* occurs in myeloid leucemia and may follow the injection of therapeutic serums.

B. Leucemia

As has been said, leucemia is a destructive process which partakes of the nature of a malignant tumor of the blood-forming tissues. Like malignant tumors, leucemia is characterized by an overproduction of immature cells, in this case immature white blood cells. There are three types of leucemia: myeloid, lymphatic, and monocytic.

Myeloid leucemia is characterized by the appearance in the blood of an excessive number of granulocytes and cells of the bone marrow from which they are derived (myeloblasts and myelocytes). The total number of leucocytes may reach 300,000 to 400,000 per c. mm. Remissions, during which the number of leucocytes returns to normal, frequently occur, but the disease finally progresses to a fatal termination. Characteristics of the disease are the high white cell count, anemia, and marked splenic enlargement.

Lymphatic leucemia is characterized by enlargement of the lymph nodes and the appearance in the blood of an abnormal number of lymphocytes and lymphoid cells from which the lymphocytes are derived (lymphoblasts). The leucocytes may reach 100,000 per c. mm. or more, and of this number from 90 to 95 per cent may be lymphocytes and lymphoblasts. The associated anemia is usually not as se-

vere in lymphatic leucemia as in the myeloid form. Like the myeloid type, lymphatic leucemia is subject to remissions during which the leucocyte count may return to normal but eventually a fatal termination ensues.

An acute leucemia partaking of the characteristics of both the myeloid and lymphatic form occasionally occurs. It is characterized by a sudden onset, fever, profound anemia, and a rapid course. *Monocytic leucemia* is usually rapidly fatal but is not of common occurrence.

C. Infectious Mononucleosis

Infectious mononucleosis is characterized by slight enlargement of the lymph nodes, mild fever, and some increase in the total number of leucocytes, with the appearance of rather characteristic white blood cells (lymphocytes) in the peripheral circulation. It may occur in epidemic form or sporadically. Although no infectious agent has been found, the course of the disease and its symptoms suggest that it is of infectious origin. *Glandular fever* is a synonym for infectious mononucleosis.

Infectious mononucleosis is important because it may be mistaken for lymphatic leucemia, and nonsyphilitic patients may give positive serological tests for syphilis during the disease and for several weeks following recovery. In addition, it may be the cause of a false positive agglutination test for typhoid fever.

III. BLOOD PLATELETS

Blood platelets are colorless objects about one-third the size of a red blood cell. Their chief function seems to be concerned with the coagulation of blood. Normally the blood contains from 250,000 to 350,000 platelets per cubic millimeter. When they fall below 60,000 per cubic millimeter, a distinct hemorrhagic tendency is present. The platelets are increased in secondary anemias, especially in those due to hemorrhage, sepsis, and myeloid leucemia. Purpura hemorrhagica, a severe form of purpura, with a marked tendency to hemorrhage from serous surfaces, is characterized by a marked reduction in platelets.

Questions for Review

1. How are red blood cells produced in the body?
2. What is the significance of the appearance of reticulocytes and normoblasts in the blood stream?
3. Anemia is characterized by what changes in the blood?
4. What are some common causes of secondary anemia?
5. What is primary anemia? Name three primary anemias.
6. How may the occurrence of erythroblastosis fetalis be explained?
7. What is meant by a differential count? What is its value?
8. Name all the different types of white blood cells. Which type comprises the largest percentage of all the white blood cells?
9. What is the characteristic white cell count of each of the following diseases: acute appendicitis, typhoid fever, whooping cough, malaria, tuberculosis?
10. Name two types of leucemia and give the symptoms of each.
11. How may infectious mononucleosis be mistaken for lymphatic leucemia?
12. What are the functions of blood platelets?

True-False Test

Place the word "true" or "false" before each statement.

- 1. Waste products are conveyed to the excretory system by the blood plasma.
- 2. In adult life red blood cells are manufactured by the red bone marrow of the long bones.
- 3. The color index in pernicious anemia is high, indicating that the hemoglobin is not reduced in as great proportion as the number of blood cells.
- 4. People suffering from pernicious anemia have a greenish color and appear undernourished.
- 5. Aplastic anemia, which is a form of anemia caused by failure of the bone marrow to produce red blood cells, may be caused by taking arsphenamine over a long period of time.
- 6. Erythroblastosis fetalis is characterized by a great increase in nucleated red blood cells.
- 7. Leucocytosis is a means of increasing the protective forces of the body.
- 8. In leucocytosis, all types of white blood cells are increased in the same proportion.
- 9. Leucemia is a disease characterized by an enormous increase in white blood cells.
- 10. In acute appendicitis, the leucocytosis is due chiefly to an increase in polymorphonuclear leucocytes.
- 11. Typhoid fever, like most other infectious diseases, is accompanied by a leucocytosis.

- 12. In pneumonia, a low leucocyte count is an unusual but favorable sign.
- 13. Whooping cough is characterized by both a leucocytosis and a lymphocytosis.
- 14. Patients with glandular fever may have a positive serological test for syphilis without having syphilis.
- 15. Purpura hemorrhagica is characterized by a very high platelet count.

References

- Gradwohl, R. B. H.: Clinical Laboratory Methods and Diagnosis, St. Louis, 1948, The C. V. Mosby Co.
- Haden, R. L.: Principles of Hematology, Philadelphia, 1946, Lea & Febiger.
- Bray, W. E.: Synopsis of Clinical Laboratory Methods, St. Louis, 1944, The C. V. Mosby Co.
- Ottenberg, Reuben: Reclassification of the Anemias, J. A. M. A. 100: 1303, (April 29) 1933.
- Fowler, Willis M.: Hematology, New York, 1945, Paul B. Hoeber Co.

CHAPTER LI

DISEASES OF THE LYMPH NODES AND SPLEEN

I. THE LYMPH NODES

A. Enlargement of the Lymph Nodes

The most common causes of lymph node enlargement may be classified as follows:

I. General enlargement.

1. Syphilis (secondary stage).
2. Leucemia (usually the lymphatic type).
3. Pseudoleucemia.
4. Status lymphaticus.
5. Certain infectious diseases (scarlet fever, measles, diphtheria, smallpox, bubonic plague).

II. Localized enlargement.

1. Nodes discrete:

1. Acute or chronic nonsuppurative lymphadenitis.
2. Early stages of Hodgkin's disease.
3. Tuberculosis of nodes.
4. Cancer of nodes.
5. Gumma of nodes.
6. Tularemia.

2. Nodes matted together:

1. Late stages of tuberculosis of nodes.
2. Advanced stages of Hodgkin's disease.
3. Suppurative lymphadenitis.
4. Lymphosarcoma.

The location of the enlarged nodes is of great importance in determining the cause of lymph node enlargement. *Enlargement of the cervical* nodes may be caused by infections of the ear, teeth, mouth, or throat, by tuberculosis, leucemia, lymphosarcoma, Hodgkin's disease, or metastatic tumors arising from areas whose drainage is received by these nodes. *Enlargement of the axillary* nodes may be caused by acute

infections of the hand, metastatic carcinoma especially of the breast (in women), leucemia, tuberculosis, metastatic melanomas, and Hodgkin's disease. *Enlargement of the inguinal nodes* may be caused by venereal diseases or other infections of the genitalia, infections of the legs, metastasis from melanomas or carcinomas (of the cervix uteri or prostate), leucemia, tuberculosis, or Hodgkin's disease. The chronically infected and enlarged lymph nodes receiving drainage from a site of long-standing infection of the lung may exert pressure on certain nerve fibers, thereby causing coughing. If there is a general adenopathy of slight degree, it is probably caused by syphilis or some other infection, while a general lymph node involvement with very large nodes is most often caused by leucemia, Hodgkin's disease, or general metastasis of tumors to the lymph nodes.

B. Lymphadenitis

Lymphadenitis, or inflammation of the lymph nodes, is caused by irritants brought to the nodes by their afferent vessels. By far the most common and important irritants are bacteria and their products. Lymphadenitis may be acute or chronic. Acute lymphadenitis may be simple (nonsuppurative) or suppurative. Acute lymphadenitis is most often observed near regions infected with pyogenic bacteria, as in the neighborhood of abscesses, acutely infected gall bladders, appendices, etc. General diseases which cause an acute lymphadenitis are typhoid fever, tularemia, and bubonic plague.

C. Tuberculosis

Tuberculosis of the lymph nodes may occur in adults but is primarily a disease of childhood. The affected nodes are at first firm and discrete. Later they become matted together, and the tubercles within the nodes fuse and become caseous. The caseous material may undergo liquefaction and be discharged on the surface by a sinus. If the caseous material does not soften, the nodes may become converted into fibrous masses by proliferation of connective tissue or undergo calcification.

Tuberculosis of the cervical lymph nodes is often referred to as *scrofula*. During the Middle Ages, scrofula was known as "the king's evil," and it was believed that a king could cure scrofula by touching the patient.



Fig. 162.—Packet of tuberculous cervical lymph nodes. Caseation has taken place. (From MacCallum: *A Textbook of Pathology*. W. B. Saunders Co.)

D. Syphilis

The nodes draining the site of a chancre are enlarged, hard, and painless. Suppuration does not occur.

In secondary syphilis there is a general enlargement of the lymph nodes which is especially evident in the epitrochlear and the superficial nodes of the back of the neck.

E. Hodgkin's Disease

Hodgkin's disease is a peculiar but rather common disease, the exact cause of which is not known, that is characterized by marked enlargement of the lymph nodes, progressive anemia, and an invariably fatal termination. It is most often a disease of young males.

Two opposing views concerning the cause of Hodgkin's disease are held by different groups of investigators. One view is that it is caused by some infectious agent. Among the infectious agents which have been proposed as the cause are *Myco. tuberculosis*, Brucella, and a virus. These claims have not been substantiated. The other theory is that it is by nature a malignant tumor. It seems that there is more evidence to support the latter theory.

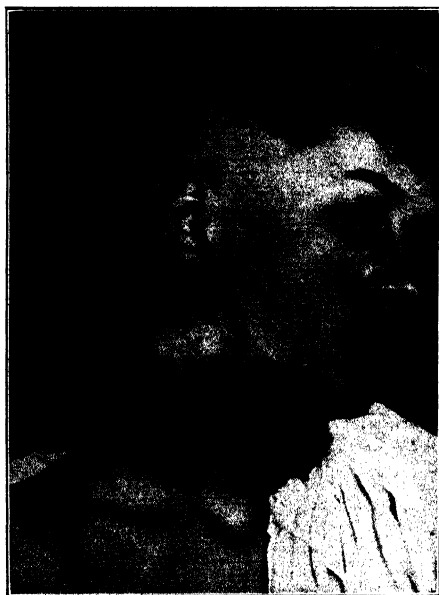


Fig. 163.—Hodgkin's disease. Note enlargement of cervical lymph nodes. (From Hertzler and Chesky: *Minor Surgery*. The C. V. Mosby Co.)

As a rule, one member after another of a group of nodes becomes involved, after which the process extends to adjoining groups of nodes or lymphoid collections. At first the nodes are discrete, but they later become matted together, and the mass reaches a disfiguring size. Hodgkin's disease most often begins as a unilateral involvement of the cervical lymph nodes.

F. Tumors

Carcinoma.—Because of the frequency with which carcinomas involve the lymph nodes receiving drainage from

the site of the tumor, it is often imperative that these nodes be removed when the tumor is eradicated. Even this often proves inadequate because by the time the carcinoma is recognized its cells have destroyed the nodes which form the first line of defense and have passed to the deeper nodes where their destruction is increasingly difficult. It should be remembered that a lymph node which is the site of a metastatic tumor may not be enlarged, and that nodes receiving drainage from a tumor site may be enlarged without being invaded by tumor cells.

Lymphosarcoma.—Lymphosarcoma, a tumor composed of lymphoid cells, is the most important primary tumor of the lymph nodes. Growth is rapid, the surrounding tissues are quickly involved, and enlargement and fusion of the nodes are marked. The outcome is uniformly fatal.

II. THE SPLEEN

The normal spleen may occasionally be ruptured by blows, falls, etc. Enlarged spleens may be ruptured by more trivial injuries. Since enlargement of the spleen forms an important physical sign, it is well to keep in mind its most important causes. An enlargement of the spleen, which is described as acute, occurs in malaria, typhoid fever, endocarditis, septicemia, pyemia, typhus fever, and plague. Chronic enlargement of the spleen may be due to passive congestion, chronic malaria, syphilis, Banti's disease, or myeloid leucemia.

Questions for Review

1. Enumerate six common causes of enlarged lymph nodes.
2. What are some common causes of lymphadenitis?
3. Why are the lymph nodes of the axillary region often removed when a breast amputation for cancer is done?
4. What are some diseases characterized by enlargement of the spleen?
5. Give etiology and symptoms of Hodgkin's disease.

True-False Test

Place the word "true" or "false" before each statement.

- 1. Tuberculosis of the lymph nodes occurs more frequently in childhood and confers an immunity to the disease in later life.

- 2. Carcinoma of lymph nodes is usually secondary.
- 3. Lymphosarcoma occurs most frequently in young people and may be primary.

References

- Boyd, William: Surgical Pathology, Philadelphia, 1947, W. B. Saunders Co.
- Rose and Carless: Manual of Surgery, New York, 1943, William Wood & Co.
- Meakins, J. C.: The Practice of Medicine, St. Louis, 1944, The C. V. Mosby Co.
- Ewing, James: Neoplastic Diseases, Philadelphia, 1940, W. B. Saunders Co.
- Miller, Richard H.: Tuberculosis of the Lymphatic System, New York, 1934, The Macmillan Co.
- Foot, N. Chandler: Pathology in Surgery, Philadelphia, 1945, J. B. Lippincott Co.
- Taylor and Nathanson: Lymph Node Metastasis, New York, 1942, Oxford University Press.

CHAPTER LII

DISEASES OF THE RESPIRATORY SYSTEM

I. THE NOSE

A. Rhinitis

Acute rhinitis may be caused by the inhalation of irritating fumes or large quantities of dust, but it occurs most often in the form of the common cold or as an accompaniment of such infectious diseases as measles, smallpox, scarlet fever, and whooping cough. Some cases are brought about by such allergic conditions as hay fever, etc.

Chronic rhinitis may be caused by repeated attacks of the acute disease, chronic sinus infections, or the continued breathing of irritating fumes or dust. It occurs in two forms: hypertrophic and atrophic. In the hypertrophic form the nasal mucosa is thickened, drainage is obstructed and polypoid outgrowths may occur. Atrophic rhinitis may follow the hypertrophic form or occur as a primary disease. In atrophic rhinitis the nasal mucosa undergoes atrophy, and the glands become inactive. In some cases ulceration, crust formation, and a fetid discharge are present. This type is known as *ozena*.

B. Tumors of the Nose

The most common "tumorlike" growth of the nose is the nasal polypus. We have used the term "tumorlike" because, although polyps are most likely inflammatory overgrowths of the nasal mucosa instead of tumors, they act mechanically like tumors by projecting into the nasal passages, producing obstruction to respiration, and interfering with the drainage of the nasal sinuses. Carcinomas, sarcomas, or other tumors of the nose may occur.

C. Adenoids

The pharyngeal tonsil is a collection of lymphoid tissue on the posterior wall of the nasopharynx. Ordinarily it increases in size until about the third year of life, after which

it remains stationary until about the age of puberty and then gradually decreases in size. If it becomes hypertrophied and obstructs the nasal passages, the condition known as *adenoids* exists. The obstruction of the respiratory passages by the pressure of adenoids brings about a characteristic train of symptoms.

Adenoids is primarily a disease of children. It is caused by irritation and inflammation brought about by such conditions as acute rhinitis and the exanthematous (accompanied by skin eruption) fevers. Adenoids are more common in cold, damp, changeable climates. In many cases it is a family characteristic.

II. THE LARYNX

Inflammations

Acute Laryngitis.—Acute rhinitis and acute laryngitis have many common causes and often occur together. Like acute rhinitis, acute laryngitis accompanies many infectious diseases. Another cause is prolonged speaking or singing. It is common for an acute laryngitis to extend to the trachea. In some cases there is considerable swelling of the laryngeal mucosa, and in children this may lead to spasmodic constriction of the laryngeal muscles, bringing about paroxysmal dyspnea and cyanosis. This is known as *spasmodic croup* and is to be differentiated from diphtheria.

Diphtheritic Laryngitis.—Diphtheritic laryngitis is usually secondary to faucial diphtheria. It is characterized by marked respiratory difficulty which may end in asphyxia.

Chronic Laryngitis.—Chronic laryngitis may follow repeated attacks of acute laryngitis, or it may be brought about by constant overuse of the voice or by the continued inhalation of irritating substances.

III. THE BRONCHI

A. Bronchitis

Acute bronchitis may involve one or both sides of the bronchial tree and may occur as a superficial inflammation limited to the larger bronchi or as an extensive inflammation in-

volving the smaller bronchi and the bronchioles. Acute bronchitis is usually of little danger except in infants, the aged, and those in a weakened condition.

Chronic bronchitis is a rather common disease that may follow influenza, bronchopneumonia, or repeated attacks of acute bronchitis, or may accompany pulmonary tuberculosis, asthma, or passive congestion of the lungs. Primary chronic bronchitis may be brought about by continued exposure to irritating dusts or fumes.

B. Bronchiectasis

Bronchiectasis is a term indicating a dilatation affecting one or more bronchi. It is usually brought about by a combination of weakening of the bronchial wall and increased intrabronchial pressure. The former is usually due to chronic inflammation and the latter to coughing or partial obstruction of a bronchus. Bronchiectasis ranks next to tuberculosis as a cause of chronic pulmonary disease.

IV. THE LUNGS

A. Circulatory Disturbances

Hemorrhage.—Hemorrhage from the lungs takes place when blood from an injured or diseased area enters a bronchus. Pulmonary hemorrhages of considerable size are most often caused by the erosion of a vessel in a tuberculous cavity which communicates with a bronchus. Less common causes are chronic passive congestion due to heart disease, injury and rupture of an aneurysm into a bronchus.

B. Emphysema

Emphysema is characterized by enlargement of the pulmonary alveoli due to stretching and breaking down of the interalveolar septa. It is usually caused by increased expiratory effort against resistance. Emphysema is best exemplified in the lungs of those who play wind instruments, glass blowers, asthmatics, and those with chronic coughs of long duration. It is also seen in the alveoli communicating with a bronchus that has become partially obstructed.

Senile emphysema is a term indicating an enlargement of the alveoli due to atrophy of their walls. It is of frequent occurrence in the aged and gives rise to few or no symptoms.

C. Atelectasis

Atelectasis is a collapsed condition of the alveoli of the lungs which may involve a portion of a lung, a whole lung, or both lungs. It may occur as a congenital condition or develop during postnatal life. In congenital atelectasis, the lung fails to expand; in postnatal atelectasis, expanded alveoli collapse. Collapse may be caused by obstruction of a bronchus, accumulation of fluid, or entrance of air into the pleural cavity. When a bronchus is obstructed, the air beyond the obstruction is absorbed by the blood and the lung collapses. Accumulation of fluid in the pleural cavity causes collapse by compressing the lung. How the entrance of air into the pleural cavity brings about atelectasis is described on page 621.

D. Pneumonia

(See pages 305 and 505.)

E. Tuberculosis

(See pages 269 and 512.)

F. Abscess of the Lungs

Abscess of the lung may be caused by the inhalation of infectious material, the deposit of bacteria within the lungs by the blood stream, or the extension of neighboring foci of suppuration. The most common cause of lung abscess is the inhalation of infectious material during operations about the nose and mouth. The next most frequent cause is some disease of the lung itself, particularly tuberculosis and pneumonia. Streptococci and pneumococci are the organisms most often found in lung abscesses.

G. Tumors of the Lung

The lung is a common site of both metastatic and primary tumors. Among the tumors that metastasize to the lungs are carcinomas (especially of the breast), sarcomas (especially

of the bones) hypernephromas and malignant melanomas. Although, up to quite recent times, it was thought that primary tumors of the lung were rare, it is now known that they are quite common and that their frequency is increasing. The most common primary tumor of the lung is carcinoma of the bronchus or bronchogenic carcinoma. This tumor is to be constantly borne in mind as a diagnostic possibility and should always be given serious consideration when a patient has an unexplained cough or pain in the chest. Benign tumors of the lung are not common.

V. SPUTUM

A. General Characteristics

Amount.—Any appreciable amount of sputum is abnormal, but a small amount may be raised by normal persons living in a highly dust-laden atmosphere. Exceptionally large amounts are expectorated in bronchiectasis, pulmonary edema, gangrene of the lungs, rupture of an abscess into a bronchus, and far-advanced pulmonary tuberculosis.

Appearance and Consistency.—Sputum may be of watery or gelatinous consistency. The tenacious character of sputum is due to its mucin content. In lobar pneumonia the sputum is often so tenacious that it will not pour out of the inverted container.

Character.—In character, sputum may be serous, mucoid, purulent, or any combination thereof, such as mucopurulent, seropurulent, etc. Serous sputum is of a thin watery consistency and is most often seen in pulmonary edema. Mucoid sputum is clear, sticky, and tenacious. It is most often seen in bronchitis. Heavy, purulent sputum usually accompanies ulceration or cavity formation. Mucopurulent sputum occurs in many conditions and is characteristic of none. Frothy sputum containing fat may be due to the lodgment of fatty emboli in the lungs.

Bloody Sputum.—The causes of bloody sputum have been given under pulmonary hemorrhage, and it is so significant of some underlying disease that its presence demands immediate investigation.

Color.—A pure mucoid sputum is transparent and colorless. Purulent sputum is usually white, gray, or green. Green sputum is due to the presence of bile or *Ps. pyocyanea*. A red or reddish brown color indicates the presence of blood or products derived from it. The rusty color of the sputum in pneumonia is due to the presence of decomposing hemoglobin. The sputum of those who live in a smoke-laden atmosphere or those who smoke and inhale may be gray or black.

Objects Found in Sputum.—*Lung stones* represent masses of necrotic tissue or inspissated exudate which have become impregnated with calcium salts and have subsequently been separated from their attachments by inflammatory processes. They are most frequently expectorated by those with tuberculosis of long duration. They may be very small or reach a diameter of one centimeter. Stones originating in the bronchi are known as *bronchioliths*; those originating in the lung tissue are known as *pneumoliths*.

Cheesy, millet seed to pea-sized objects may occur in the sputum of those with acute progressive or far-advanced tuberculosis. These objects may contain myriads of tubercle bacilli.

Bakers may expectorate doughy masses; cotton mill workers may expectorate masses, a large portion of which is cotton. Foreign bodies, such as bits of cloth, shot, etc., may accidentally gain access to the lung and subsequently be expectorated.

B. The Sputum in Disease

Tuberculosis.—Instead of the sputum's being characteristic in tuberculosis it shows the widest variation. In the incipient stage of the disease no sputum may be expectorated, or it may be very scanty and of a grayish yellow or white color. As the disease progresses the amount of sputum increases until in the far-advanced stages great quantities may be expectorated.

It should be remembered that the failure to find tubercle bacilli in the sputum does not necessarily mean that the disease does not exist because the bacilli may be absent even

though the disease is far advanced. It should also be remembered that one specimen of sputum may show the bacilli in abundance and a few or none be found in a specimen taken a few days later. Tuberculous lesions not communicating with a bronchus will not show tubercle bacilli in the sputum. Such lesions are known as "closed lesions."

In *lobar pneumonia* the sputum is scanty and tinged with blood (rusty). It is highly tenacious and is often expectorated with difficulty. Many pneumococci are usually present.

In *pulmonary gangrene* the sputum is of a dirty brown color and has an offensive odor.

In *bronchial asthma* the sputum is at first scanty, clear, and grayish in color. Later it is frothy and microscopically shows the structures known as "Curschmann's spirals" and "Charcot-Leyden crystals."

VI. THE PLEURA

A. Hydrothorax, Hemothorax, Pneumothorax

The occurrence of fluid, blood, or air in the pleural cavity is known as hydrothorax, hemothorax, and pneumothorax, respectively.

Hydrothorax may be a part of the generalized dropsy of heart or kidney disease.

Hemothorax may be caused by wounds of the chest, malignant tumors of the lungs or pleura, tuberculous pleurisy, or the rupture of an aneurysm into the pleural cavity.

Pneumothorax may be caused by penetrating wounds of the chest wall or the establishment of a communication between the pleural sac and a bronchus. When air enters a pleural sac, the negative pressure which is maintained in the sac, allowing the air within the lung to keep the lung distended, is released, and the lung collapses. In some cases so much air enters the sac that neighboring organs are pushed aside and the opposite lung is compressed.

B. Pleuritis

Pleuritis or *pleurisy*, as it is commonly called, is inflammation of the pleura. It may be caused by generalized infections

or by the extension of local infections. Among the general infections that may be complicated by pleuritis are septicemia, pyemia, and such infectious diseases as acute rheumatic fever. Among the local conditions, the extension of which may lead to pleuritis, are the pulmonary lesions of pneumonia, tuberculosis or influenza, gangrene of the lung, pericarditis and, less often, inflammatory conditions of the liver. Pleuritis may also occur as a result of penetrating wounds of the chest. The most frequent causative organisms are streptococci, pneumococci, and *Myco. tuberculosis*. *The tuberculous nature of all pleuritis arising without apparent cause should be suspected.*

Pleurisy occurs in three major forms: fibrinous, sero-fibrinous, and purulent. The second form often represents a progression of the first, and the third often represents a progression of the second, but each may possess its own distinctive features from the beginning. The process is at first localized, but due to the respiratory movements it soon extends and involves both surfaces of the pleura.

Questions for Review

1. What is rhinitis?
2. What is bronchiectasis? What are some common causes of this condition?
3. Describe the changes which take place in the lungs in emphysema.
4. Describe the lung changes in atelectasis.
5. Name several diseases characterized by the raising of large amounts of sputum.
6. What is the significance of bloody sputum?
7. Describe the sputum characteristic of lobar pneumonia.
8. Discuss the sputum in tuberculosis.
9. What are lung stones? How are they formed?
10. Define: hydrothorax, hemothorax, pneumothorax.
11. What are some common causes of pleurisy?
12. Name three types of pleuritis.

True-False Test

Place the word "true" or "false" before each statement.

- 1. The raising of sputum is abnormal.
- 2. The sputum raised by a person suffering with bronchiectasis is scanty and very tenacious.
- 3. Bloody sputum is always indicative of tuberculosis.

- 4. Rusty sputum is due to the presence of old blood and is often seen in pneumonia.
- 5. Failure to find the tubercle bacillus in several specimens of sputum proves that there is no tuberculosis present.

References

- Pottenger, F. M.: Tuberculosis of the Child and Adult, St. Louis, 1934, The C. V. Mosby Co.
- Gradwohl, R. B. H.: Clinical Laboratory Methods and Diagnosis, St. Louis, 1948, The C. V. Mosby Co.
- Anderson, W. A. D.: Synopsis of Pathology, St. Louis, 1946, The C. V. Mosby Company.
- Meakins, J. C.: The Practice of Medicine, St. Louis, 1944, The C. V. Mosby Co.
- Cecil, Russell L.: Textbook of Medicine, Philadelphia, 1947, W. B. Saunders Co.

CHAPTER LIII

DISEASES OF THE NERVOUS SYSTEM

I. THE MENINGES

A. Hemorrhage

Meningeal hemorrhage may be extradural (between the dura and bone) or subdural (between the dura and pia-arachnoid; i.e., in the subdural space).

Extradural hemorrhages are due to direct or indirect injuries which separate the dura from the bone and rupture one or more blood vessels. Unrelieved, severe extradural hemorrhages may cause death.

Subdural hemorrhage is usually due to direct or indirect blows with or without fracture of the skull and is the most common type of traumatic intracranial hemorrhage. The hemorrhage may come from the large venous sinuses, the large arteries, or the cerebral veins.

Bleeding is much more rapid in subdural than in extradural hemorrhage and in severe cases immediate death may occur.

Hemorrhages beneath the pia-arachnoid are known as *sub-arachnoid* hemorrhages. They are most often due to laceration of the brain.

B. Purulent Meningitis

The organisms most often responsible for purulent meningitis are the meningococcus (see page 334), pneumococci, streptococci, influenza bacilli, colon bacilli, typhoid bacilli, and *Ps. pyocyanea*. Of these, meningococci, pneumococci, and streptococci are the most important. The bacteria may reach the meninges in several different ways, the most important of which are: (1) by wounds, (2) by passage from the nasopharyngeal mucosa by way of the lymph spaces, (3) by extension of infections of the middle ear, mastoid process, the bony sinuses or cranial bones, and (4) by the blood stream.

Pneumococcus meningitis may be due to the extension of a pneumococcus infection of the middle ear or mastoid process,

or it may complicate lobar pneumonia. *Streptococcus meningitis* may be a complication of such systemic diseases as measles, endocarditis, septicemia, facial erysipelas, etc., or it may be due to the extension of an infection of the middle ear, mastoid process, or frontal sinus, etc. Meningitis due to *Bact. typhosum* occurs most often as a complication of typhoid fever. Purulent meningitis is a frequent complication of sinus thrombosis.

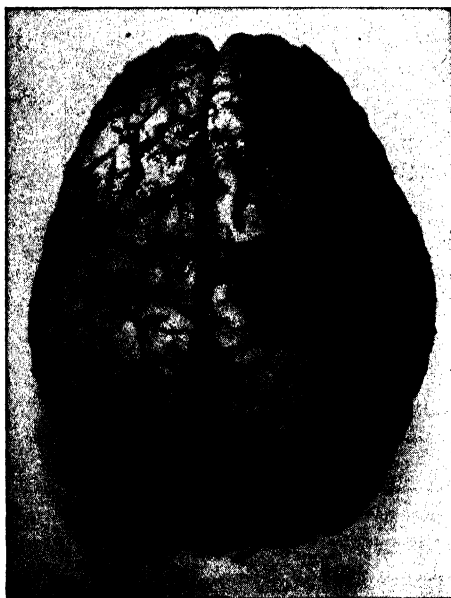


Fig. 164.—Subarachnoid hemorrhage. The black area on the right is the site of hemorrhage. (From Anderson: Synopsis of Pathology.)

In suppurative meningitis the blood shows a marked increase in polymorphonuclear leucocytes and lumbar puncture reveals a cerebrospinal fluid, the characteristics of which are detailed on page 637.

C. Tuberculous Meningitis

Tuberculous meningitis is characterized by a well-marked inflammatory reaction of the meninges with which the formation of few or many tubercles is associated. It is usually a disease of childhood but may occur in adults. It is most often

a part of a generalized miliary tuberculosis but may be due to bacilli brought to the meninges by the blood stream from distant foci, or it may be due to direct extension from adjacent foci, such as the bones of the skull or spinal column.

As a rule, the tubercles are more numerous on the meninges covering the base of the brain, but the meninges of the entire brain may be involved and tubercles may be found on the lining of the ventricles and within the substance of the brain. An accumulation of fluid in the ventricles in tuberculous meningitis is so common that the disease has been called acute hydrocephalus.

Tuberculous meningitis differs from purulent meningitis in that it is of longer duration, and the cerebrospinal fluid is seldom purulent. The disease is uniformly fatal.

D. Syphilitic Meningitis

Syphilitic meningitis or cerebral syphilis, more properly called meningovascular syphilis, is a syphilitic involvement of the meninges and vessels of the central nervous system with or without involvement of its parenchymatous tissue. It is the most common of the manifestations of neurosyphilis.

While not all patients with syphilis develop meningovascular involvements, a goodly percentage (20 to 30 per cent) do. It usually develops within the first five or six years after infection but may develop as early as two months or as late as forty years. The meninges may be slightly thickened or show no change. The vascular changes consist of a thickening of the walls and a weakening of the vessels. Thrombus formation or vascular rupture leading to hemiplegia may occur.

II. THE BRAIN

A. Injuries

1. CEREBRAL CONCUSSION

When a person receives an injury of the head, he may become groggy for a time and quickly recover, or he may sink into a state of unconsciousness with subnormal tempera-

ture and scarcely perceptible respiration and pulse that may, on rare occasions, end in death from respiratory failure. When this condition of widespread loss of cerebral control follows the mere reception of an injury, without any explanatory lesions, such as a fracture of the skull, hemorrhage, or tearing of the brain tissue being present, it is known as *cerebral concussion*, or concussion of the brain.

Various theories have been proposed to explain cerebral concussion. One is that it is due to a molecular disturbance of the brain tissue. Another is that it is due to suddenly induced cerebral anemia, and still another is that the jar accompanying the injury drives the cerebrospinal fluid from the lateral and third ventricles into the fourth ventricle with such force that it paralyzes the cardiac and respiratory centers situated in the floor of the latter.

After concussion the patient may manifest symptoms of irritability for a long time or be permanently impaired. In some cases memory of the injury and the events immediately preceding it are completely wiped out.

2. COMPRESSION

Any condition that reduces the capacity of the skull or increases the volume of the brain or the amount of fluid in the cranial cavity increases intracranial pressure and compresses the brain. Among these causes are: (1) hemorrhage, (2) inflammation, (3) edema, (4) tumors, and (5) fractures with marked depression of the internal or all tables of the skull. The most common cause is hemorrhage.

The rapidity with which symptoms develop depends on the rapidity with which the compression develops, which in some cases is a matter of seconds and in others a matter of months. The first symptoms to develop are headache, vomiting unrelated to the taking of food, drowsiness, slow pulse, and high blood pressure, increased spinal fluid pressure, and choked disks. As the pressure increases, the patient has convulsions and becomes stuporous and comatose, with Cheyne-Stokes respiration and incontinence of feces and urine. The deepening coma may end in death from respiratory failure.

B. Circulatory Disturbances

1. HYDROCEPHALUS

Situated on the walls of the lateral ventricles of the brain are little tufts of delicate capillaries known as choroid plexuses through which the components of the cerebrospinal fluid are transferred from the blood plasma to the ventricles.



Fig. 165.—Child with hydrocephalus. (From Meakins: Practice of Medicine, The C. V. Mosby Co.)

From the ventricles the fluid passes through three small openings in the roof of the fourth ventricle to the subarachnoid space. If there is some obstruction to the passage of the fluid from the ventricles to the subarachnoid space, the ventricles become widely dilated, and the overlying brain tissue becomes reduced to a thin layer. This is known as *hydrocephalus*. From the clinical standpoint hydrocephalus may

be classified as congenital (occurring at birth or before ossification has begun) and acquired (occurring after ossification has begun).

In congenital hydrocephalus the enlargement of the head may be so great during intrauterine life that birth is rendered impossible. More often the head is little larger than normal at birth but enlarges so rapidly after birth that the child dies within a few weeks.

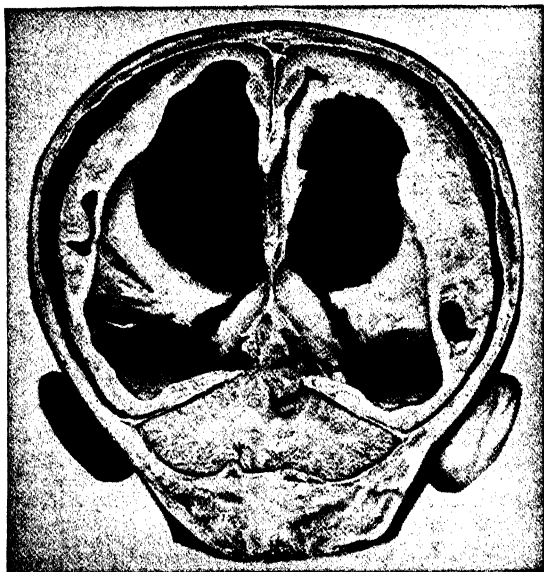


Fig. 166.—Section through the skull and brain of a child with chronic hydrocephalus, showing extreme distention of the lateral ventricles. (Beattie and Dickson.)

Acquired hydrocephalus is due to an obstruction of the circulation of the cerebrospinal fluid by adhesions, especially those due to septic or tuberculous meningitis, or the growth of tumors. Since bony union has progressed to some degree or is complete before acquired hydrocephalus begins, the skull does not show the marked enlargement seen in congenital hydrocephalus and, of course, the ventricles are not so widely dilated but there is a terrific increase in intracranial pressure.

Extreme degrees of hydrocephalus are incompatible with life. In moderate degrees the patient may be able to lead a fairly active life and the mentality remains unaffected, but this is not the usual case.

2. CEREBRAL HEMORRHAGE

Although there are many types of intracranial hemorrhage due to many different causes, the one that is of greatest importance is the spontaneous hemorrhage due to vascular disease that occurs in the brain substance and is the chief cause of the clinical condition known as *apoplexy*.

The symptoms of brain hemorrhage depend on the size of the hemorrhage, the rapidity of its formation, and its location. Large hemorrhages which involve vital centers may cause immediate death. When immediate death does not occur, the patient gradually or suddenly becomes unconscious and may have convulsions. At the height of the attack the patient is in profound coma with flushed face, stertorous breathing, and incontinence of feces and urine. If the coma does not end in death, consciousness gradually returns after hours or days but the patient is usually left with one or more disabling after-effects, the most important of which is paralysis. Whatever the outcome of a given attack, the underlying cause remains, and the hemorrhages will recur until one proves fatal.

3. THROMBOSIS AND EMBOLISM

Emboli derived from the left side of the heart in acute endocarditis or chronic valvular disease, or from destructive lesions of the lungs, often lodge in the cerebral vessels. Thrombosis of the cerebral vessels may be due to arteriosclerotic or syphilitic changes, or it may follow the lodgment of an embolus or accompany certain infectious diseases or blood dyscrasias.

In both thrombosis and embolism the mass of brain supplied by the occluded vessel dies and becomes converted into a liquid producing the condition known as *encephalomalacia* or softening of the brain. The functional disturbances are

similar to those of brain hemorrhage. Like cerebral hemorrhage, both thrombosis and embolism are followed by paralysis. Fat embolism may be the cause of widespread convulsive symptoms and may quickly prove fatal.



Fig. 167.—Apoplexy, both fresh and healed. The large, fresh hemorrhage has burst into the ventricle. The old one is represented by a cavity with pigmented walls in the substance of the opposite hemisphere. There is a small clot in the ventricle of that side. (From MacCallum: *A Textbook of Pathology*. W. B. Saunders Co.)

C. Inflammations

1. ENCEPHALITIS

Strictly speaking, the term “encephalitis” denotes any inflammation of the brain, but by common usage it has come to denote the more diffuse inflammations of the brain in contradistinction to a localized inflammation or brain abscess.

In addition to the epidemic type of the disease there are other types of encephalitis which may be due to a variety of causes. It may form a prominent complication of typhus fever, diphtheria, scarlet fever, measles, whooping cough,

influenza, typhoid fever, or malaria. In at least some of these the encephalitis may not appear until the primary infection has subsided. In malaria the encephalitis is due to plugging of the cerebral capillaries by agglutinated parasites. A frequent cause of encephalitis is the direct extension of some other intracranial infection; e.g., meningitis. Other causes are syphilis, miliary tuberculosis and arsenic, lead or alcohol poisoning. It may follow the extraction of septic teeth or occur during pregnancy or shortly after delivery. Encephalitis related to pregnancy usually improves when the uterus is emptied, but sometimes the opposite is the case.

The onset of encephalitis is usually sudden, with irritability followed by stupor, stiffness of the neck, localized paralysis and in some cases, convulsions. If recovery occurs, the patient may be left with such after-effects as paralysis, epileptiform convulsions, and slight or extensive mental changes. Epidemic and postvaccinal encephalitis were discussed on page 377.

2. BRAIN ABSCESS

Brain abscesses are most often due to staphylococci, streptococci, pneumococci, or *Ps. pyocyanea*, which reach the brain through wounds or extension from neighboring foci of suppuration, such as the middle ear, mastoid process, or bony sinuses, or they are brought to the brain from distant foci by the blood stream. The most common cause of brain abscess in civil life is suppuration of the middle ear or mastoid process. Brain abscesses are usually single but may be multiple. Multiple abscesses are usually of embolic origin.

Symptoms may develop with such rapidity that in order to save the patient's life immediate attention is demanded, or the abscess may lie dormant for months or years before it gives rise to symptoms. The most common symptoms of chronic brain abscess are loss of weight, decrease in appetite, and the signs of cerebral compression. Slight fever and a moderate leucocytosis are often present. Various types of paralysis or convulsive attacks may point to the location of the abscess. Mental signs suggestive of hysteria, changes in character, or psychoses may be present. Most brain abscesses ultimately end fatally.

D. General Paresis

General paresis (general paralysis of the insane; paralytic dementia) is a diffuse meningoencephalitis that is due to the *Treponema pallidum* and is characterized by a progressive dementia and general paralysis terminating in death. It is one of the three important forms of neurosyphilis (see page 523) and occurs in about 3 per cent of patients who have syphilis. It is more common in highly civilized than in primitive races; and in civilized races, it is more common in the educated than in the ignorant. Excessive mental work or strain and alcoholism are predisposing factors. Although the incidence of syphilis is high among Negroes, paresis is of infrequent occurrence. Its frequency in males is about five times as great as in females.

Juvenile paresis, which ordinarily begins between the twelfth and eighteenth years, is a rather common complication of congenital syphilis and usually lasts from two to five years after the onset of symptoms.

E. Epilepsy

Epilepsy is not a definite disease entity, but, like jaundice and dropsy, is a condition that may be due to several different causes.

The typical epileptic seizure begins with a loss of consciousness with which there is associated extreme pallor of the face and hands. The loss of consciousness is followed by a phase of general muscular rigidity during which respiration ceases, the tongue is bitten, and the normal color of the face returns and progresses to cyanosis. Muscular rigidity then abates and violent convulsive movements of the body begin. During the convulsive attacks the patient makes peculiar sounds, and a clear or bloody froth exudes from the mouth. After the attack is over the patient remains in a condition of stupor or complete exhaustion for a few minutes. Epilepsy associated with attacks such as this is known as *grand mal*. When the patient merely loses consciousness for a few seconds, it is known as *petit mal*.

As a rule, the epileptic shows mental deterioration and is despondent, hypersensitive, disagreeable, and suspicious. Memory of the attack is usually completely effaced.

There are so many theories as to the cause of epilepsy that it would be beyond the scope of this book even to mention them. It will be said, however, that there are many causes of the disease and epileptics usually show signs of some hereditary physical or psychic degeneration.

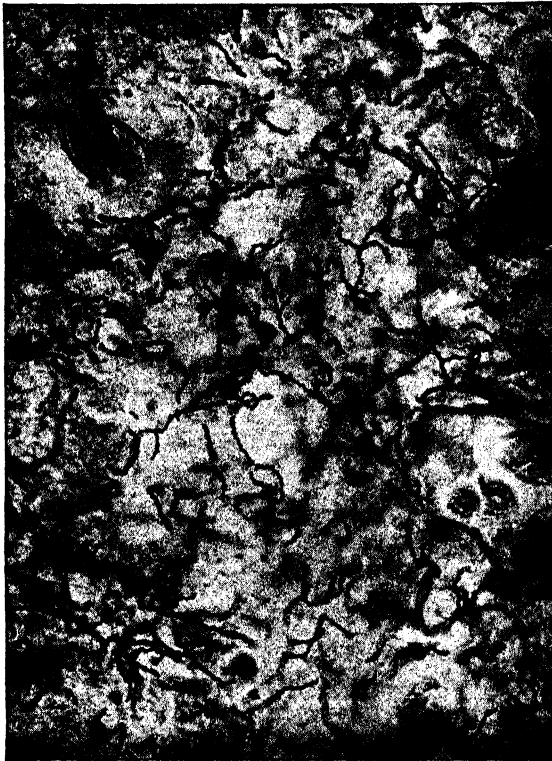


Fig. 168.—*Treponema pallida* in the brain of a patient with general paresis. Compare with Fig. 97, page 393. (From Grinker: *Neurology*. Courtesy of Charles C Thomas, Publisher, Springfield, Ill.)

F. Brain Tumors

Included within the term “brain tumor” are all tumors arising within the cranial cavity regardless of whether they arise primarily from the brain substance, bone, or other intra-

cranial structures. The majority, however, arise within the brain substance and about 40 per cent are gliomas, i.e., tumors arising from the supporting tissue of the nervous system. There seems to be a more definite relation existing between traumatism and brain tumors than between traumatism and tumors in other parts of the body.

Brain tumors, as a whole, show little tendency to metastasize to distant parts of the body and some have little tendency to invade the surrounding tissue, but they are of extreme danger on account of the increase in intracranial pressure which they produce. Some brain tumors kill within a few months, while in other cases the patient lives for several years.

Spinal punctures may end disastrously in a brain tumor because the cerebrospinal fluid pressure is so high that the cerebellum becomes engaged in the foramen magnum when the pressure in the vertebral canal is released.

Closely related to brain tumors are the retinal gliomas which are usually locally destructive. They have a familial incidence and usually occur before the child is four years of age. In 20 per cent of cases tumors occur in both eyes. The outcome is usually fatal.

III. THE SPINAL CORD

A. Poliomyelitis

(See Microbiology, page 375.)

B. Tabes Dorsalis

Tabes dorsalis or locomotor ataxia is a degeneration of the posterior columns of the spinal cord and the posterior nerve roots and ganglia caused by *Treponema pallidum*. It is one of the three important forms of neurosyphilis.

Since the disease attacks the sensory pathways of the cord, its manifestations are chiefly those of incoordination and disturbances of sensation. Among the common manifestations are: (1) pain, (2) ataxic gait, (3) visceral crises, (4) loss of sensation and reflexes, (5) optic atrophy, (6) disturbances of sphincters, (7) Romberg's sign, and (8) Argyll Robertson pupil.

IV. THE CEREBROSPINAL FLUID

A. Characteristics of Normal Fluid

Normal cerebrospinal fluid is a clear, colorless sparkling liquid with a specific gravity of about 1.001 to 1.008. The normal cell count ranges from 1 to 5 cells per c. mm. More than 10 cells per c. mm. should be regarded as distinctly abnormal. The protein content of normal spinal fluid is so low that its presence can hardly be detected by the tests ordinarily used. Cerebrospinal fluid contains about one-half as much sugar and slightly more chlorides than the blood.

The pressure exerted by the cerebrospinal fluid is influenced by so many factors that readings made on different subjects or the same subject at different times show considerable variation. Factors influencing it are the age of the patient, position of the patient when reading is made, coughing, crying, etc. With the patient in the recumbent position the pressure in children ranges from 45 to 90 mm. of water, and in adults it ranges from 130 to 150 mm.

B. Pathological Changes in the Cerebrospinal Fluid

Color and Appearance.—Pathological spinal fluid may be yellow or blood tinged. Yellow fluids may be found in certain types of tumor of the cord or may be a late result of hemorrhage.

Turbid fluids usually indicate a purulent meningitis and call for immediate bacteriological investigation. The fluid is clear or at the most only slightly opalescent in tuberculous meningitis, syphilis of the central nervous system, encephalitis, and poliomyelitis.

Blood may be found in the cerebrospinal fluid as a result of old or recent hemorrhage, or it may be accidentally introduced during the puncture. If the blood imparts a dark red or brown color to the fluid an old hemorrhage is indicated. Fresh blood suggests a recent hemorrhage or its accidental introduction during the puncture. If the blood is due to hemorrhage it will be uniformly mixed with the specimen. If it is accidentally introduced it will be more abundant in the

first few drops of fluid removed. Fractures of the skull will not give a bloody spinal fluid unless the meninges are torn, and a cerebral hemorrhage will not cause a bloody fluid unless it breaks into a ventricle or opens upon the surface of the brain.

Cells.—An increase in cells accompanies almost any inflammatory condition of the central nervous system. When the cell count reaches 200 per c. mm., a distinct turbidity is present. An increase in cells is most marked in the acute types of meningitis, and the majority of the cells are polymorphonuclear leucocytes. There is some increase in cells, and the lymphocyte is the predominating cell in tuberculous meningitis, poliomyelitis, encephalitis, and syphilitic involvements of the central nervous system.

The *sugar* content of the fluid is decreased in meningitis, increased in encephalitis, and normal in poliomyelitis.

Chlorides are decreased in meningitis, especially the tuberculous type, and are within normal limits in poliomyelitis and encephalitis.

C. Cerebrospinal Fluid Changes in Diseases of the Central Nervous System

Purulent Meningitis.—In acute purulent meningitis the cerebrospinal fluid pressure is greatly increased, but the fluid may contain so much pus that it will scarcely flow from the needle. In appearance the fluid is opalescent or distinctly turbid and often has a green or yellow hue. The cells of the exudate are chiefly polymorphonuclear leucocytes and thousands may be present. In most cases of purulent meningitis the causative organisms may be easily demonstrated by smears made from the fluid, but occasionally cultures are necessary. The fluid sugar shows a marked reduction, and there is a considerable decrease in chlorides.

Tuberculous Meningitis.—In tuberculous meningitis the fluid is usually transparent but may be opalescent. The cells range from 30 to 150 per c. mm. The majority are lymphocytes. Chlorides show a marked decrease and sugar is moder-

ately decreased. A painstaking study of slides carefully prepared from the fluid will often reveal tubercle bacilli.

Poliomyelitis.—In the beginning of poliomyelitis the cell count ranges from normal to 200 per c. mm., and the majority are lymphocytes. Sugar and chlorides are usually within normal limits. After paralysis begins, the fluid gradually returns to normal.

Encephalitis.—In epidemic encephalitis the cerebrospinal fluid is usually clear but may be slightly opalescent. The cells range from normal to 200 or 300 per c. mm. Sugar is normal or increased, and the chlorides show little change. This is of value in differentiating encephalitis from tuberculous meningitis. In the latter sugar and chlorides are both reduced in amount.

Neurosyphilis.—In all types of syphilitic involvement of the central nervous system the cerebrospinal fluid is under increased pressure, proteins are increased, and the number of cells is higher than normal. In paresis and tabes dorsalis the cell count ranges from 50 to 100 per c. mm. It may be higher in meningovascular syphilis. Lymphocytes are the predominating cells. All types of neurosyphilis give a positive Wassermann test of the fluid and in most cases a positive test is also obtained on the blood. The colloidal gold test gives a characteristic curve in paresis.

Brain Abscess.—In the early stages of brain abscess the cerebrospinal fluid is clear, but a slight increase in cells may be present. At a later stage the abscess may give rise to a meningitis or may rupture and its contents become mixed within the fluid.

Tumors of the Brain and Cord.—In brain tumor the cells are slightly increased in number, and there is some increase in proteins. When tumors of the cord completely obstruct the flow of cerebrospinal fluid, the fluid shows one or more of the changes characterized as Froin's syndrome. These changes are: (1) a yellow coloration of the fluid, (2) high protein content with slight or no increase in cells, and (3) massive coagulation of the fluid. Of these signs the second is most important and most uniformly present.

Questions for Review

1. By what routes may the bacteria causing purulent meningitis reach the meninges?
2. What are often the primary sources from which a pneumococcus meningitis originates?
3. Give some of the theories of the cause of cerebral concussion.
4. What two underlying conditions may act as causes of cerebral compression? Give some of the symptoms of cerebral compression.
5. Give some of the symptoms and discuss the outcome of a spontaneous cerebral hemorrhage.
6. Give some of the causes of encephalitis.
7. What organisms are most often the cause of brain abscess? How may they reach the brain?
8. What types of people are most likely to develop general paresis?
9. What is the difference between grand mal and petit mal?
10. Why may a spinal puncture sometimes end disastrously when a brain tumor is present?
11. What are the three important forms of neurosyphilis? Which is most common?
12. What are some of the signs of tabes dorsalis?
13. What does fresh blood in the cerebrospinal fluid indicate?
14. Discuss the Wassermann reaction on the cerebrospinal fluid in syphilis of the central nervous system.

True-False Test

Place the word "true" or "false" before each statement.

- 1. Extradural hemorrhage is the most common form of traumatic cerebral hemorrhage but never causes death.
- 2. The cerebrospinal fluid is usually purulent in tuberculous meningitis.
- 3. All patients with syphilis eventually develop the meningo-vascular form of the disease.
- 4. Any degree of hydrocephalus is incompatible with life.
- 5. There is only one type of encephalitis.
- 6. Negroes have general paresis more often than white people because they have syphilis more often.
- 7. Epilepsy is not a definite disease and is due to many causes.
- 8. Brain tumors usually cause death but seldom spread to distant parts of the body.
- 9. More than ten cells per cubic millimeter of cerebrospinal fluid is abnormal.
- 10. The pressure of cerebrospinal fluid shows considerable variation under different conditions.

- 11. Turbid cerebrospinal fluid indicates an inflammatory condition of the meninges.
- 12. A fracture of the skull does not cause blood to appear in the cerebrospinal fluid unless the meninges are torn.

Completion Test

1. The organisms most often responsible for purulent meningitis are _____, _____, and _____.
2. Tuberculous meningitis is usually a disease of _____ but may occur in _____.
3. The most common cause of cerebral compression is_____.
4. The components of the cerebrospinal fluid are transferred from the blood plasma to the ventricles of the brain by the_____
5. The symptoms of brain hemorrhage depend on the_____of the hemorrhage, the_____with which it is formed, and its _____.
6. Brain abscesses are usually_____but may be_____.
7. General paresis and tabes dorsalis are both caused by_____.

References

- Wechsler, Israel S.: Textbook of Clinical Neurology, Philadelphia, 1947, W. B. Saunders Co.
- Boyd, William: A Textbook of Pathology, Philadelphia, 1947, Lea & Febiger.
- Foot, N. Chandler: Pathology in Surgery, Philadelphia, 1945, J. B. Lippincott Co.

CHAPTER LIV

DISEASES OF THE DIGESTIVE SYSTEM

I. THE LIP, MOUTH, AND TONGUE

A. Stomatitis, Glossitis, and Gingivitis

The terms "stomatitis," "glossitis" and "gingivitis" indicate an inflammation of the mouth, tongue, and gums respectively. These conditions are so closely related, both from the standpoint of etiology and clinical manifestations, that a brief description of the most common types will be substituted for any attempt at discussing them systematically.

Catarrhal Stomatitis.—Catarrhal stomatitis is a superficial nonulcerative inflammation of the mouth. It may be caused by mechanical, thermal, chemical, or bacterial irritants. Possibly some cases which occur when the body is below normal are of an infectious nature, and this explains why catarrhal stomatitis often occurs during the course of typhoid fever, measles, gastric disorders, and diabetes.

Aphthous (Phlyctenular or Vesicular) Stomatitis.—In this condition small white spots lying on an inflamed base occur, especially on the lower lips and gums. These are the "stomach sores" of the layman. The etiology of this type of stomatitis is not known, but it very common in teething children who live in unhygienic surroundings or are suffering from debilitating diseases. In adults aphthous stomatitis may be associated with digestive disturbances, and in women it may occur at each menstrual period or during pregnancy or the puerperium.

Ulcerative Stomatitis.—This type of stomatitis which may be due to many different causes is characterized by profuse salivation, offensive breath, and the presence of areas of ulceration which most often begin on the margins of the gums and spread to the adjacent mucosa. It occurs most often in **unclean mouths with neglected teeth**. After the ulcers have extended to a certain point, they become covered with a dirty

grayish pseudomembrane. In some cases the ulceration may be so extensive as to cause loosening of the teeth.

Causes of ulcerative stomatitis other than the organisms which produce the specific type of the disease known as "trench mouth" are poisoning by mercury, lead, copper, or phosphorus. It may also occur during exanthematous diseases, grave nutritional disturbances, or in poorly nourished children. One of the most common forms of ulcerative stomatitis is mercurial stomatitis which follows the taking of mercury compounds, or occurs in those whose occupation exposes them to mercury. The stomatitis is brought about by the elimination of mercury in the saliva.

Trench Mouth.—See Microbiology, page 398.

Thrush (Parasitic Stomatitis).—See Microbiology, page 413.

B. Syphilis of the Lip and Oral Cavity

The lip is the most common site of extragenital chancres, and occasionally a chancre occurs within the oral cavity.



Fig. 169.—Chancre of the tongue. (Courtesy of Dr. Grover W. Wende. Sutton and Sutton: *Diseases of the Skin*. The C. V. Mosby Co.)

Chancres of the lip and oral cavity are usually contracted by kissing or the use of infected eating utensils.

Mucous patches occur almost exclusively in the mouth and are among the most infectious of all syphilitic lesions. They

occur during the secondary stage of the disease as well-circumscribed, whitish, slightly raised lesions and are most numerous on the inside of the lips and along the edges and on the surface of the tongue. (See Plate XII.) White star-shaped scars at the angles of the mouth are strong evidence of syphilis, especially the congenital type.

C. Tumors of the Mouth

In addition to cancers various tumors, such as angiomas, papillomas, and fibromas, may occur in the mouth, and solid or cystic tumors may arise in connection with the teeth.

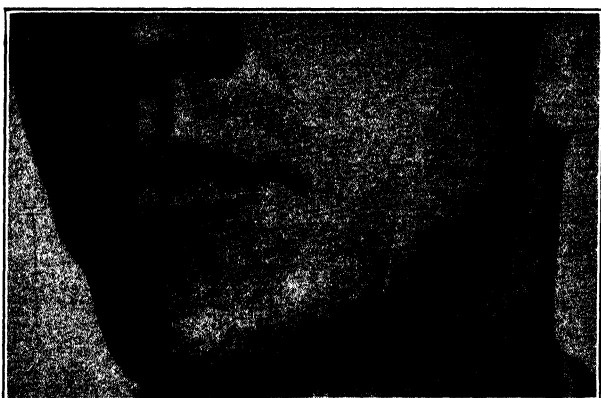


Fig. 170.—Early cancer of the lower lip. (From Hertzler and Chesky: *Surgery of a General Practice*. The C. V. Mosby Co.)

Cancer of the Lip.—Cancer of the lip usually occurs in males over forty years of age. It begins as a thickened nodule, papillary growth, or ulcer. As a rule, the point of origin is the mucocutaneous junction about halfway between the midpoint of the lower lip and the angle of the mouth. If ulceration is not present at first, it finally occurs and the lesion does not heal at all or else repeatedly heals and breaks down. The irritation produced by hot pipe stems and jagged teeth is an important causative agent. In untreated cases death usually occurs within one to three years.

Cancer of the Tongue.—Cancer usually begins on the edge of the anterior two-thirds of the tongue. The chronic irrita-

tion produced by tobacco smoke, jagged teeth, etc., is a predisposing cause. The disease is characterized by its rapid course and high mortality.

Cancer in other parts of the mouth may follow the irritation produced by jagged teeth or ill-fitting dentures. Leucoplakia is an important predisposing cause. Metastasis is rapid and death occurs early.

Epulis or Giant Cell Tumor.—This tumor which is improperly called “giant cell sarcoma” is of common occurrence and arises from the alveolar process of the jaw. It is a hard, slow-growing tumor which causes considerable enlargement of the jaw and disturbance of the surrounding tissues but seldom recurs after removal.

II. THE THROAT

A. Pharyngitis

Pharyngitis (inflammation of the pharynx) often represents the extension of rhinitis and nasopharyngitis. From the pharynx the infection may extend to the larynx. Like rhinitis and nasopharyngitis, pharyngitis may be acute or chronic.

B. Retropharyngeal Abscess

By the term *retropharyngeal abscess* is meant an abscess in the loose tissues between the posterior pharyngeal wall and the vertebral column. Retropharyngeal abscesses may be acute or chronic. The former usually represents the extension of a phlegmonous pharyngitis, while the latter usually occurs as a complication of tuberculosis of the cervical vertebrae. Acute retropharyngeal abscess is characterized by marked prostration, extensive swelling, pain on swallowing, loss of voice, and inability to open the mouth. The mortality is high and death usually occurs as a result of suffocation.

C. Tonsillitis

Catarrhal Tonsillitis.—The cause and symptoms of catarrhal tonsillitis are the same as those of catarrhal inflamma-

tions in general. As a rule, the local symptoms are mild and constitutional symptoms may be absent.

Lacunar Tonsillitis.—In this condition which is improperly called follicular tonsillitis there is an acute inflammation of the tonsil with plugging of the crypts by exfoliated epithelial cells, leucocytes, and bacteria. The plugs project from the mouths of the crypts and appear on the surface of the tonsil as multiple white patches. The causative organisms are usually streptococci or staphylococci. One tonsil may be affected before the other or the disease may remain confined to a single tonsil.

Chronic Tonsillitis.—Chronic tonsillitis is most often due to repeated attacks of acute tonsillitis and may occur as a (1) lacunar tonsillitis, (2) hyperplastic tonsillitis, or (3) fibrous tonsillitis. *Chronic lacunar tonsillitis* possesses many of the characteristics of the acute form and like many other chronic conditions may be considered a prolongation of the acute form. *Hyperplastic tonsillitis* is characterized by a marked hyperplasia of the lymphoid tissue of the tonsils which may be so great that the tonsils almost touch each other. While this type of tonsillitis gives rise to the greatest enlargement of the tonsils, it usually causes the least systemic disturbance. *Chronic fibrous tonsillitis* is characterized by the replacement of the lymphoid tissue of the tonsils by connective tissue. This type of tonsillitis causes only moderate enlargement. The contraction of the connective tissue often produces atresia of the crypts, and the enclosure of organisms within the crypts often leads to the formation of intra-tonsillar abscesses from which infection spreads to other parts of the body.

D. Diphtheria

(See pages 285 and 519.)

E. Vincent's Angina

(See Microbiology, page 398.)

F. Septic Sore Throat

(See Microbiology, page 322.)

III. THE ESOPHAGUS

A. Stenosis—Strictures

Stenosis of the esophagus may be caused by (1) strictures resulting from the swallowing of hot liquids or corrosive chemicals, (2) obstruction or strictures produced by tumors, (3) lodgment of foreign bodies within the esophagus, and (4) external pressure by tumors, enlarged lymph nodes, goiters, pericardial effusions, or an enlarged heart. When the esophagus is injured to such an extent that ulceration occurs, the ulcer heals with the formation of a scar, and if the ulceration has been extensive enough, the contraction of the scar produces a stricture. *Strictures* may be single or multiple and are particularly extensive after the swallowing of corrosive poisons. The accidental swallowing of commercial lye is the most common cause of esophageal stricture in children. In the beginning, esophageal stenosis is characterized by slight difficulty in swallowing solids. As the stenosis progresses the difficulty increases until at last the patient is unable to swallow either solids or liquids and death from starvation occurs.

B. Tumors

Benign tumors of the esophagus are comparatively rare. Cancer of the esophagus is fairly common and is among the most hopeless of diseases. The first symptom of esophageal cancer is usually slight difficulty in swallowing. Death ordinarily occurs within eighteen months after the onset and is most often due to perforation into a respiratory passage followed by pneumonia, pulmonary gangrene, or lung abscess.

IV. THE STOMACH AND DUODENUM

A. Congenital Defects

Congenital Hypertrophic Stenosis.—Congenital hypertrophic stenosis, the most important congenital defect of the stomach, is characterized by spasms and hypertrophy of the ring of muscle fibers surrounding the pylorus. The hypertrophy and spasms may be so great that the pyloric passage is almost completely occluded, and the mass of hypertrophied

muscle fibers can be palpated through the abdominal wall. The cause of the disease is not known. As a rule, no symptoms are present at birth and the infant does well for the first two to four weeks of life, at which time, without apparent cause, vomiting begins. The child vomits after taking food, and the vomiting ceases as soon as the stomach is empty. As the stenosis progresses the vomiting becomes worse, until all food is vomited as soon as taken. The stomach becomes dilated and hypertrophied to four or five times its normal size, and its attempts to force food through the pyloric opening may be so intense that the child cries with pain and the peristaltic waves of the stomach can be seen to pass across the abdominal wall. The child quickly begins to suffer from starvation and unless relieved soon dies.

B. Gastric Hemorrhage

Gastric hemorrhages of considerable size are usually due to cancer, ulcer, or intense passive congestion, especially passive congestion secondary to heart disease or cirrhosis of the liver. The coffee-ground vomitus due to partially digested blood is particularly significant of gastric cancer but may occur in gastric ulcer or other diseases of the stomach. Dangerous hemorrhages secondary to portal obstructions may occur from a ring of varicose veins at the cardiac end of the stomach.

It is sometimes necessary to determine whether bloody material was vomited or came from the lungs. In hematemesis the reaction of the material is usually acid and hydrochloric acid may be detected by chemical tests, while material from the lungs is alkaline in reaction and does not contain hydrochloric acid. Blood of gastric origin may have the coffee-ground appearance referred to above, while blood of pulmonary origin is frothy and is of a bright red color.

C. Peptic Ulcer

Peptic ulcers occur almost exclusively in the stomach (especially the pyloric end) and the first part of the duodenum. On account of the part accorded the gastric juice in the production of these ulcers, they have been called peptic

ulcers in recognition of the action of pepsin, the most important enzyme of the gastric juice.

Many theories of the causation of peptic ulcers have been proposed and most are based on the assumption that in some manner a circumscribed portion of gastric mucosa becomes devitalized and is subsequently digested by the gastric juice. Just how devitalization occurs is not known, but it seems to be a frequent complication of extensive burns, septicemia, etc., because these conditions are often complicated by peptic ulcer.



Fig. 171.—Chronic ulcer of stomach. (From Anderson: Synopsis of Pathology.)

Peptic Ulcer of the Stomach (Gastric Ulcer).—Acute gastric ulcers are usually multiple and vary from pinhead size to an inch in diameter. In many cases no symptoms are present and the ulcers heal without leaving a scar, while in other cases perforation or a fatal hemorrhage may occur. Chronic gastric ulcers are usually single and are most often from one to two inches in diameter. Hemorrhage is frequent and perforation may occur, but in most cases perforation

is prevented by the formation of adhesions between the base of the ulcer and the adjacent organs and tissues. In some cases the contraction of the scar of a healed ulcer leads to a stenosis of the pylorus.

Duodenal Ulcer.—It was formerly thought that duodenal ulcers were not as common as gastric ulcers, but they are now known to be more common. Ulcers of the duodenum are confined almost entirely to the portion receiving the acid gastric chyme. They may be acute or chronic and like gastric

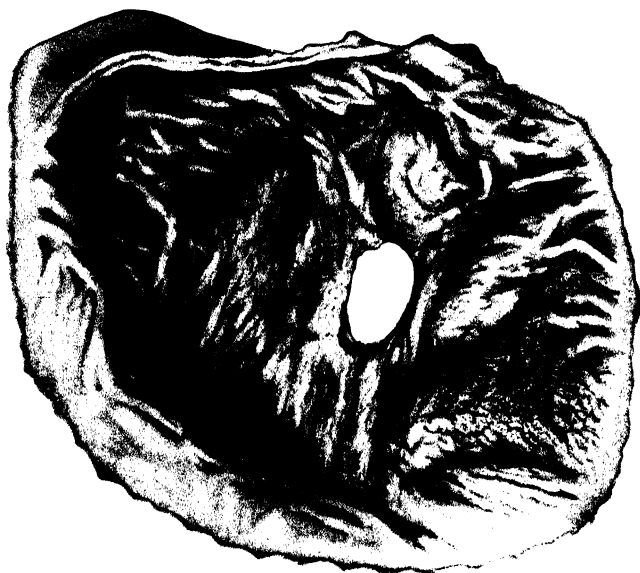


Fig. 172.—Perforated gastric ulcer. (From Karsner: *Human Pathology*. J. B. Lippincott Co.)

ulcers, acute duodenal ulcers are often multiple. Perforation of acute duodenal ulcers is more common than perforation of acute gastric ulcers. The symptoms of duodenal ulcer are much like those of gastric ulcer, and the clinical differentiation of the two is often difficult.

In some cases the hemorrhage from a peptic ulcer may be of such severity as to cause death. In hemorrhages of moderate severity the patient feels a sudden pain and becomes faint, and after a few hours passes one or more tarry stools.

Perforation is indicated by sudden intense pain, shock, and rigidity of the abdominal muscles. Without immediate treatment the patient dies of general peritonitis within twenty-four to forty-eight hours.

D. Cancer

The stomach is a rather common site of cancer. Many observers believe that ulcers strongly predispose to cancer and that from 10 to 20 per cent of all gastric ulcers undergo



Fig. 173.—Carcinoma of stomach with ulceration and thickened, elevated margin. (From MacCallum: *A Textbook of Pathology*. W. B. Saunders Co.)

cancerous degeneration. Other workers are in direct opposition to this view, believing that ulcers thought to undergo cancerous degeneration are cancers from the beginning.

Cancer of the stomach is more common in men than in women and usually occurs after the fortieth year. The disease seems to be especially prevalent in certain families.

Cancer usually affects the pyloric end of the stomach. It may occur as (1) a large fungating mass projecting into the cavity of the stomach, (2) as an ulcerated area with a crater-like appearance, or (3) as a diffuse infiltration of the stomach wall. The first type is usually the least dangerous because it does not invade the stomach wall deeply or metastasize early, and on account of its large size is rather easily recognized.

Among the local effects of cancer of the stomach are hemorrhage, perforation, and pyloric stenosis. The latter aided by fermentation of the stagnated stomach contents leads to marked dilatation of the stomach. In some cases a general invasion of the wall of the stomach with marked proliferation of connective tissue leads to the production of linitis plastica or "leather bottle stomach."

Gastric cancer extends by continuity to the liver, pancreas, gallbladder, and other near-by structures. It may metastasize to the peritoneum and ovaries. In some cases the metastasis of malignant cells by way of the thoracic duct leads to enlargement of the supraclavicular lymph nodes on one or both sides.

E. Gastric Contents

In normal persons the amount of gastric juice excreted each day probably lies between 1,500 and 3,000 c.c. The rate of secretion and the composition of the juice depend on several factors, important among which are the health of the person, the presence of food in the stomach, and certain psychic influences as hunger, fear, mental anxiety, etc. This has given rise to two methods of examining the gastric contents: (1) the examination of the fasting contents and (2) the examination of the contents after the ingestion of a test meal.

At the height of digestion the gastric contents consist of (1) water, (2) pepsin, (3) hydrochloric acid, (4) rennin, (5) certain mineral salts, (6) products of digestion, and (7) undigested food. In addition to these, gastric lipase (a fat-

splitting enzyme) and organic acids may be present. Hydrochloric acid is of special importance in gastric physiology because it promotes the digestive action of pepsin (a protein-splitting enzyme), which is the most important digestive enzyme of the stomach. Hydrochloric acid occurs in two forms: "combined" and "free." When food is in the stomach, a portion of the hydrochloric acid secreted enters



Fig. 174.—Introducing nasal tube to remove stomach contents.

into combination with the protein portion of the food to form protein salts of hydrochloric acid. This is known as "combined acid." When the affinities of the proteins of the food have been satisfied the acid appears in the "free" or uncombined state. In gastric analysis, therefore, we speak of combined hydrochloric acid, free hydrochloric acid, and total acidity. The last represents the total of the combined hydrochloric acid, free hydrochloric acid, and all other acids and

acid salts that may be present. Each is measured in terms of the amount of decinormal alkali required to neutralize the particular type of acid in 100 c.c. of gastric contents. This is spoken of as *degrees* of acidity. The amount of free hydrochloric acid is of by far the greatest diagnostic significance.

The average volume of the fasting stomach contents is from 40 to 50 c.c. If the volume is more than 150 c.c., a hypersecretion of gastric juice or an inability of the stomach to empty itself is indicated. Normal fasting contents have an average total acidity of 30 degrees and an average free hydrochloric acid content of 17.5 degrees.

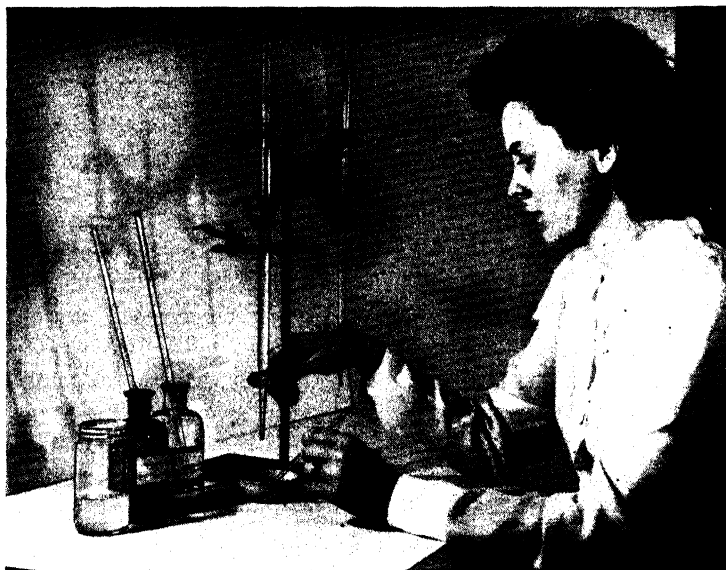


Fig. 175.—Technician titrating stomach contents to determine how much acid is present.

Ordinarily from 50 to 100 c.c. of gastric contents may be removed at the end of an hour after a test meal. At this time the total acidity normally ranges from 50 to 75 degrees, the free hydrochloric acid from 25 to 50, and the combined from 10 to 15 degrees.

An increased amount of free hydrochloric acid in the stomach contents is known as *hyperchlorhydria*, a decreased amount as *hypochlorhydria*, and an absence as *achlor-*

hydria. Hyperchlorhydria is practically always present in early cases of gastric ulcer but may occur in other conditions, such as chronic gastritis, gallstones, etc. In cancer of the stomach and pellagra, free hydrochloric acid is usually reduced in amount or is absent. In pernicious anemia it is absent in practically every case.

Causes of blood in the stomach contents other than the ones given on page 647 are the accidental swallowing of blood from the gums, etc., and injury produced by the stomach tube. Blood due to traumatism from the stomach tube is usually of a bright red color and occurs in streaks.

The Boas-Oppler bacillus is the only organism of special significance encountered in the gastric contents. It occurs in most cases of cancer of the stomach and is seldom found in other conditions.

Since gastric ulcer and cancer are of such common occurrence and gastric analysis is so often resorted to when either is suspected, it is desirable to review the gastric findings in the two conditions. In gastric cancer the free hydrochloric acid is usually below normal or is absent. It may occasionally be normal in amount but is seldom above. Those cases showing a very low or absent free hydrochloric acid usually also show the presence of lactic acid and Boas-Oppler bacilli. In ulcer the amount of free hydrochloric acid is usually high and, of course, no lactic acid or Boas-Oppler bacilli are present.

V. THE INTESTINES

A. Congenital and Acquired Abnormalities of Shape and Position

Diverticula.—Diverticula may be congenital or acquired. The most important congenital diverticulum is *Meckel's diverticulum* which arises from the small intestine. Acquired diverticula may arise from either the small or large intestine but are more common and larger in connection with the latter (especially the descending colon).

Meckel's diverticulum which is due to an incomplete obliteration of the primitive yolk stalk arises from the ileum about 18 inches above the cecum. It shows considerable varia-

tion in size and shape, but in most cases it occurs as a thumb-like process extending from the intestine and measures from one to three inches in length. Meckel's diverticulum is of danger because it may become inflamed (giving symptoms much like those of appendicitis), ulcerated, or perforated. A diverticulum may become wrapped around an intestine and cause strangulation.

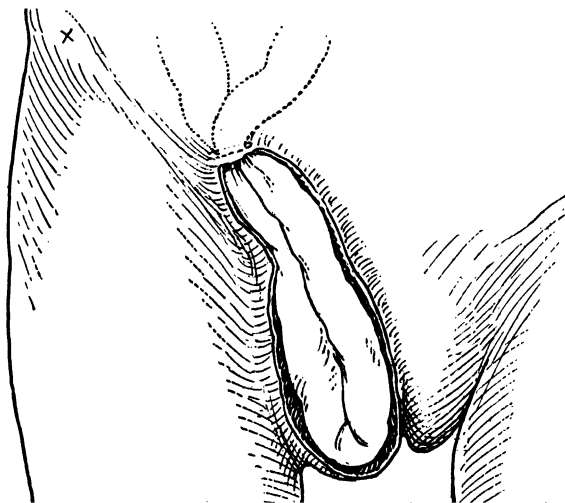


Fig. 176.—Diagrammatic illustration of an inguinal hernia in a woman. The hernia has descended into the labium majus. (From Crossen and Crossen: *Diseases of Women*.)

Hernia.—The term “hernia” in its broader sense means the protrusion of a viscus through an opening in the cavity that contains it. The term, however, usually takes on a more restricted meaning and refers to the protrusion of a part of an intestine (usually the small intestine) or some other abdominal viscus through an opening in the abdominal wall. In this chapter we will discuss hernia in the restricted meaning. A hernia may be caused by the passage of an abdominal viscus through (1) an opening that has closed insufficiently or one that has closed sufficiently but is congenitally weak (inguinal, femoral, and umbilical hernias), (2) openings brought about by injuries that disrupt the continuity of the abdominal wall, or (3) a weakened point resulting from a

failure to restore completely the integrity of the abdominal wall after an operation.

A typical hernia consists of a *sac* which represents a pouch-like protrusion of the peritoneum and the *hernial contents* which usually consists of intestine, omentum, or both intestine and omentum. Inguinal, femoral, and umbilical hernias are most common. *Inguinal* hernias are of two types: the "indirect," in which the components of the hernia enter the inguinal canal by way of the internal abdominal ring and leave by way of the external abdominal ring to descend into the scrotum, and the "direct," in which the viscus passes directly through the abdominal wall and emerges from the external abdominal ring where it appears under the skin or passes to the scrotum. In women, inguinal hernias pass to the labia majora. In *femoral hernias* the hernia protrudes from the femoral ring and presents on the inside of the thigh. *Umbilical hernias* occur in infants as a result of imperfect closure of the abdominal wall at the umbilicus. A *diaphragmatic hernia* represents an upward displacement of an abdominal viscus through an acquired or congenital opening in the diaphragm.

In a general way it may be said that a hernia is caused by the forcing of a portion of the abdominal contents into the hernial opening by single or repeated exposures to increased intra-abdominal pressure. In the first case the hernia comes on suddenly as after a strain, while in the latter it comes on more gradually.

When the hernial contents can be returned to their normal position within the abdominal cavity, the hernia is said to be *reducible*. A hernia may be rendered irreducible by inflammatory adhesions between the hernia and surrounding structures, or one containing intestine may be rendered irreducible by the collection of feces or undigested food in the lumen of the portion of intestine entering into the formation of the hernia. A hernia which has been rendered irreducible by the collection of feces or undigested food material in the lumen of the intestine without any disturbance of blood supply is said to be *obstructed*. When the blood supply of a hernia is cut off, the hernia is said to be *strangulated*. Ob-

structed hernias should be subjected to immediate operation because they always quickly become strangulated. Strangulation, an ever present danger in all hernias, is quickly followed by congestion, swelling, and paralysis of the bowel with resulting gangrene and peritonitis.

B. Wounds and Ruptures of the Intestines

Rupture of the intestine may be produced directly by blows on the abdomen or indirectly by blows on the back, falls, etc., and in many cases no sign of external injury is present. The sign of intestinal perforation or rupture are profound shock, abdominal rigidity, vomiting, and pain. If the patient survives the shock, peritonitis follows.

C. Communicable Diseases Affecting the Intestines

1. Typhoid fever (See page 510).
2. Bacillary dysentery (See page 512).
3. Amebic dysentery (See page 427).
4. Tuberculosis (See page 512).

D. Intestinal Obstruction

By *intestinal obstruction* is meant a partial or complete occlusion of the bowel with interference with the passage of its contents. The obstruction may be acute or chronic and may affect the large or small intestine. Acute obstruction is practically always accompanied by blocking of the blood supply of the affected segment of the intestine. This is known as *strangulation*. Many of the symptoms of acute intestinal obstruction are due to the accompanying strangulation and, as will be shown later, blocking of the blood supply to a segment of intestine may, within itself, cause obstruction.

The causes of intestinal obstruction may be classified as mechanical and paralytic. The mechanical causes may be further classified as those brought about by (1) changes involving the intestinal wall (strangulation of hernias, intussusception, volvulus, and the contraction of scars from ulcers), (2) outside pressure (from bands, adhesions, tumors or misplaced organs), and (3) obstruction within the lumen (tumors, polyps, concretions, intestinal parasites, and foreign bodies).

In paralytic obstruction the affected segment becomes paralyzed on account of the blocking of its blood or nerve supply. Since the paralyzed segment is unable to pass its contents, the bowel is just as truly obstructed as if it were mechanically obstructed. Paralytic obstruction is often spoken of as paralytic *ileus*. The large intestine tolerates obstruction much better than the small intestine and complete obstruction of the large intestine, without strangulation, may exist for several days without causing symptoms.

Acute Intestinal Obstruction.—*Acute mechanical obstruction* is most often caused by strangulation of hernias, pinching of segments of intestine by bands or adhesions, intussusception, or volvulus. As a rule, carcinoma of the colon eventually causes acute obstruction. Bands which bring about obstruction may be congenital but are usually of inflammatory origin. The manner by which bands most often promote obstruction is by the slipping of a coil of intestine into an opening made by a band passing from the bowel to the mesentery.

Paralytic obstruction, which is always acute, is most often caused by peritonitis and is known to complicate fractures of the rib and infectious conditions, such as pneumonia. Less often it is due to mesenteric thrombosis or occurs as a post-operative complication, especially when the handling of the intestines has not been gentle enough or has been prolonged. On rare occasions it occurs without known cause.

Acute intestinal obstruction usually comes on with lightning-like rapidity and practically never occurs without strangulation. At first there is a violent peristalsis above the obstruction. This gives rise to most intense pain. Shock, vomiting, and abdominal rigidity with paralysis and dilatation of the bowel follow. Serum pours into the distended bowel and bacteria multiply in its stagnated contents; these combine to increase the distention. The vomiting increases and becomes fecal, and the patient goes into collapse. The intestinal wall becomes black and gangrenous. If actual rupture does not occur the intestinal wall becomes permeable to bacteria, and a most violent peritonitis speedily develops and rapidly proves fatal. The higher in the intestinal tract the obstruction, the more severe and rapidly fatal it is.

Chronic Intestinal Obstruction.—*Chronic intestinal obstruction* differs from acute obstruction in that in the former there is no interference with the blood supply. If the blood supply becomes blocked during the course of a chronic obstruction, the obstruction becomes acute. Chronic obstruction may be caused by the growth of tumors in the intestinal wall, the gradual contraction of scars, etc. Chronic obstruction is always incomplete, and when it becomes complete the symptoms of acute obstruction develop, but in the case of the large bowel the obstruction may be complete several days before the symptoms appear.

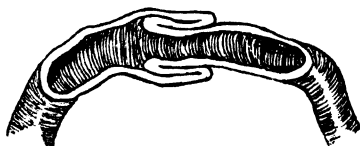


Fig. 177.—Section of intestine showing intussusception. (From Zahorsky and Zahorsky: *Synopsis of Pediatrics*. The C. V. Mosby Co.)

Intussusception.—By intussusception, the nature of which can be much better described by a picture than by words, is meant the slipping of a portion of intestine into the succeeding portion. Intussusception is said to be brought about by increased peristalsis of the segment which becomes invaginated or atony of the portion which receives it.

As the upper segment slips into the lower, the bowel is obstructed and the mesentery is pulled in between the two layers of intestine and pinched, so that from the very beginning both obstruction and strangulation exist. When acute intussusception occurs, the classical symptoms of obstruction appear. A chronic form of intussusception which may end in acute obstruction occasionally occurs in adults.

Volvulus.—By volvulus is meant the twisting of a loop of intestine on its long axis or the rotation of a loop of intestine to such an extent that its mesentery becomes twisted. In either case interference with the blood supply of the affected segment leads to paralytic obstruction, gangrene, and peritonitis. The disease occurs most often in elderly persons and the pelvic colon is the most common site.

E. Cancer of the Intestine

Cancer of the intestine, exclusive of cancer of the rectum, is neither as common nor as malignant as cancer in other parts of the gastrointestinal tract. At first cancer of the intestine may be symptomless, but the obstruction brought about by the tumor leads to increasing constipation. As the constipation increases, pain sets in, and the section of bowel above the tumor dilates. The irritation produced by the hardened masses of feces causes inflammation of the intestine which leads to attacks of diarrhea that interrupt the constipation. These attacks are characteristic features of the disease. Cancer of the intestine usually leads to acute intestinal obstruction.

F. Intestinal Protozoa

The most important protozoon of the intestinal tract is *Endameba histolytica*, the cause of amebic dysentery (see page 427). In addition, many ciliates and flagellates that are definitely nonpathogenic or whose pathogenicity is questioned are found in the intestinal canal.

G. Feces

Feces is a mixture of (1) undigested food remains, (2) partially digested food and products of digestion, (3) products added by the activity of the digestive tract, such as bile, pancreatic enzymes, etc., (4) decomposition products, (5) epithelial cells, (6) bacteria, and (7) water. The normal offensive odor of the stool is due to the decomposition products, indol and skatol.

Color.—Normally the stool is of a light or dark green color due to urobilin, which is derived from bilirubin, one of the bile pigments. Changes in color may be caused by diet, drugs, or disease. A meat diet gives a dark color; milk gives a yellow color, and following a vegetable diet the stool is of a dark brown color. Calomel gives a green stool, while following the ingestion of bismuth salts the stool is black. Clay or putty colored stools occur when the amount of bile or pancreatic juice delivered to the intestine is deficient. The

color is due to an abnormally large amount of undigested fat. Green stools occur in the diarrheas of children but may occur in apparently healthy persons. Stools containing large amounts of pus or mucus may be gray in color. The color imparted by blood will be discussed later.

Mucus.—Mucus may occur intimately mixed with the stool, on the outside of it or may form casts of the intestine. An excessive amount is always abnormal and indicates an irritation or inflammation. In dysentery, ileocolitis, and intussusception, the stools may consist entirely of blood-streaked mucus. Mucous casts may be mistaken for tapeworms.

Blood.—Blood may occur in the feces as a result of disease in any part of the alimentary tract. In some cases it can be detected by gross observation, while in others its detection depends on chemical tests (occult blood). Macroscopic blood (detected by gross observation) may occur as streaks on the surface of the stool or intimately mixed with it, giving the stool a tarry black, brown, or red color. Tarry black colorations are due to the digestive action of the intestinal enzymes on the blood and indicate that the hemorrhage came from high in the alimentary tract (throat, esophagus, stomach, or small intestine). A red or brown color indicates that the hemorrhage came from the lower bowel. If a diarrhea is present, blood from high intestinal hemorrhages may be of a red color because it is swept along so swiftly that it is little affected by the digestive enzymes. Blood streaks on the outside of the stool indicate rectal or anal lesions, such as ulcers, fissures, or hemorrhoids. As a general rule it may be said that if the extraneous sources of blood, such as bleeding gums and blood ingested in the food are excluded, blood in the feces indicates either cancer or ulcer of the stomach or tumors or ulcerative lesions of the intestine.

Concretions.—Gallstones are of frequent occurrence in the feces. They can often be identified by their faceted surfaces. Chemical tests may be resorted to as a means of further identification. Nodules of fat or soap, which frequently appear in the feces after taking oil, should not be mistaken for gallstones.

H. Intestinal Worms

Tapeworms.—Tapeworms have a larval and an adult cycle of existence. As a rule, the two cycles occur in different species of animals. The adult cycle occurs in the intestinal canal and the larval cycle occurs within the tissues of the body. The host in which the larval cycle of a development takes place is known as an *intermediate* host. The one in which the adult worm exists is known as a *definitive* host. Of course, the tapeworms which interest us here are those whose adult cycle occurs within the intestinal canal of man.

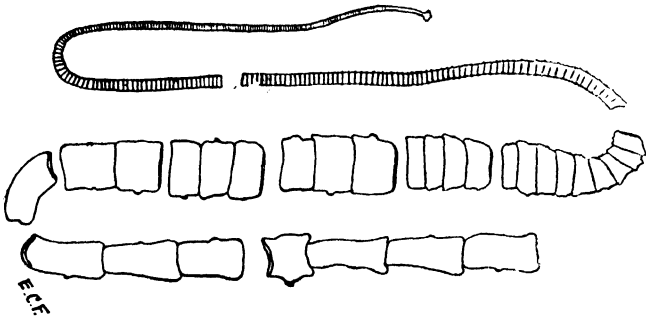


Fig. 178.—Portions of a tapeworm. Note the very small head. (From Faust: *Human Helminthology*. Lea and Febiger.)



Fig. 179.—Head of a tapeworm. (From Gay and Associates: *Agents of Disease and Host Resistance*. Courtesy of Charles C Thomas, publisher, Springfield, Illinois.)

Adult tapeworms have a small head and a nonsegmented neck, spoken of collectively as the *scolex*, to which are attached in linear arrangement a variable number of segments. New segments are formed from the scolex and the youngest segment is the one nearest the scolex, while the segment farthest away is the oldest. Up to a certain point the farther the segment is from the scolex the larger it is. After this

point is reached, the segments become smaller on account of degenerative changes. The head of a tapeworm is very small in comparison with the remainder of the body, often being no larger than a pinhead. It is provided with suckers, hooklets, or both, for attachment to the intestinal wall. The different species of tapeworms vary from one centimeter to ten meters in length.



Fig. 180.—Portion of tapeworm (*Taenia saginata*) expelled after treatment. The length of the portion expelled is about 2 meters. The head is not present.

Regardless of how many segments are obtained, treatment which fails to remove the head is of no value, because the head will replace the lost segments.

The cycle of development of tapeworms is as follows: the eggs are expelled with the feces and swallowed by a sus-

PLATE XXI.—OVA OF INTESTINAL PARASITES

1. *Ascaris lumbricoides* (fertilized egg).
2. *Ascaris lumbricoides* (unfertilized egg).
3. *Necator americanus* (late segmentation).
4. *Necator americanus* (four-cell stage).
5. *Oxyuris vermicularis*.
6. *Trichuris trichiura*.
7. *Ascaris canis*.
8. *Diphyllobothrium latum*.
9. *Taenia saginata*.
10. *Ehabditis hominis*.
11. *Hymenolepis nana*.
12. *Hymenolepis diminuta*.
13. *Schistosoma mansoni*.
14. *Fasciolopsis buski*.

(From Bray: *Synopsis of Clinical Laboratory Methods*, The C. V. Mosby Co.)

ceptible intermediate host; the gastrointestinal juices digest the "shells" of the eggs and set the larvae free. The larvae penetrate the intestinal wall and are carried to different parts of the body by the blood stream; when they lodge in the fleshy parts of the body, the tissues form a cyst wall around them. If raw or insufficiently cooked flesh containing the cysts is eaten by a suitable definitive host, the cyst walls are digested and the larvae attach themselves to the intestinal wall of the new host and develop into adult worms. As a rule, the eggs of adult worms may be found by microscopic examination of the feces.

Taenia saginata (beef tapeworm) is a common parasite of man. Usually, only one worm is present. The cow and the giraffe are the intermediate hosts. This parasite may reach a length of ten meters.

Infestation with *Taenia solium* (pork tapeworm) is infrequent in America. It is acquired by eating infected pork. Only one worm is usually present. This worm is from two to eight meters in length.

Taenia nana is the smallest and most common tapeworm of man. It measures from one to four centimeters in length and many worms are present. The exact details of the life history of *Taenia nana* are not known.

Infestation with the fish or broad Russian tapeworm is of rather frequent occurrence in America.

Hookworm.—*Ankylostoma duodenale* and *Necator americanus* are respectively the Old World and New World hookworm. They bear a close resemblance to each other but differ in several details. The adult *Necator americanus* is from seven to eleven mm. in length, and the mouth is provided with hooklets for attachment to the intestinal wall. Many worms inhabit the small intestine. They are not passed in the feces unless active purgation is present, but eggs in abundance are practically always present.

The life history of the hookworm is as follows: after the ova are passed in the feces and deposited in the open, development begins and the larvae hatch out. When the larvae come in contact with the skin (usually of the feet), they penetrate it, producing a dermatitis ("toe itch" or "ground itch").

The larvae then pass by the lymph and blood stream to the lungs. In the lungs they gain access to the bronchi and are conveyed to the pharynx and swallowed. After reaching the small intestine they develop into adult worms. No intermediary host takes part in the life cycle of this parasite.

Strongyloides Intestinalis.—Infestation with *Strongyloides intestinalis* is very common. The adult worm is about 2 cm. in length. Larvae are fairly plentiful in the feces, but neither adult worms nor eggs are present in the absence of active purgation.

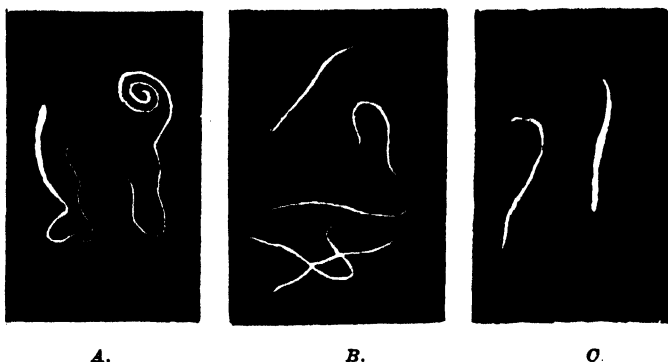


Fig. 181.—Intestinal worms frequently found in children. A., whipworm (actual size). B., Oxyuris (actual size). C., hookworm (enlarged). (From Zahorsky and Zahorsky: *Synopsis of Pediatrics*.)

Ascaris Lumbricoides (Eelworm, Roundworm).—This is the largest intestinal nematode (roundworm). It is fusiform in shape and bears a close resemblance to the common earthworm. Its habitat is the upper end of the small intestine. Several are usually present, and they may knot together and form palpable masses or produce intestinal obstruction. Infestation is most common in children under ten years of age.

Oxyuris Vermicularis (Threadworm, Pinworm, Seatworm).—This parasite is most often seen in small children. The adult worms migrate through the anus and deposit their eggs around the anal margin. This occurs at night and is accompanied by intense itching. The worm may invade the vagina and urethra.

Trichocephalus Dispar.—*Trichocephalus dispar* (whipworm) is of frequent occurrence but does not produce marked symptoms.

Flukes.—Flukes are flat, leaflike, nonsegmented parasites which are not of frequent occurrence.

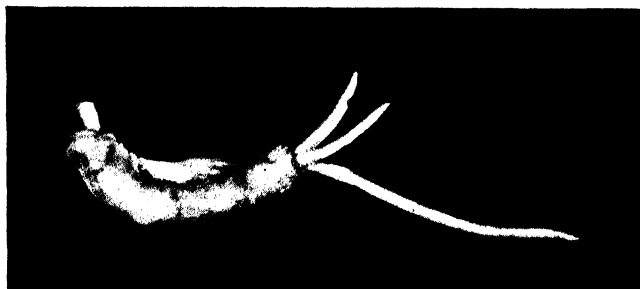


Fig. 182.—Roundworms extending through the perforation at end of appendix. The patient, a four-year-old child, had the symptoms of a fulminating appendicitis. Postoperative recovery occurred in a normal manner. (Courtesy Mother Frances Hospital, Tyler, Texas.)

I. Intestinal Bacteria

About one-third of the weight of the feces is due to its bacterial content. These bacteria fall into two classes: (1) those which are so frequently present as to be regarded as normal inhabitants, and (2) pathogenic bacteria which gain access to the intestinal canal. Of the first group more than fifty species have been studied. In the second group are found the typhoid and paratyphoid bacilli, the dysentery bacilli, the organism of Asiatic cholera, and the tubercle bacillus.

VI. THE VERMIFORM APPENDIX

Appendicitis

Appendicitis (inflammation of the appendix) usually begins in the mucosa and spreads to the other layers of the appendix. The bacteria that most often cause appendicitis are *Bact. coli*, staphylococci, and streptococci. Of these *Bact. coli* is the most common. These bacteria usually reach the wall of the appendix by way of its lumen but occasionally reach it by way of the blood stream. Appendical infections due to

streptococci are especially severe and are often complicated by widespread peritonitis. Certain anaerobic bacteria which are normal inhabitants of the intestine may act as secondary invaders in acute appendicitis.

In addition to the large amount of lymphoid tissue in the mucosa, the dependent position of the appendix renders it liable to infection, and the poor blood supply of the organ predisposes to gangrene. Inflammation of the appendix is likely to be especially severe because the swelling of the mucosa may occlude the lumen and convert the portion of the lumen distal to the occlusion into a closed cavity. When occlusion from any cause occurs, bacteria in the resulting cavity undergo rapid multiplication.



Fig. 183.



Fig. 184.

Fig. 183.—Acute appendicitis with peritoneal exudate. Note the swollen appearance. (From Boyd, William: *Surgical Pathology*. W. B. Saunders Co.)

Fig. 184.—Acute appendicitis with perforating ulcer. (From MacCallum: *A Textbook of Pathology*. W. B. Saunders Co.)

When our knowledge of appendicitis was more limited than now, it was thought that the disease was caused by the lodgment of foreign bodies, such as seeds, shot (from game), etc., in the lumen of the appendix. It is now known

that most of these so-called foreign bodies are fecal concretions. Fecal concretions are not accorded the importance as causative agents of appendicitis that they once were. However, their contents may infect the mucosa, or they may obstruct the lumen of the appendix or exert such pressure on its mucosa that ulceration and thrombosis are produced.

Appendicitis is rare in infancy and old age. The disease is confined almost exclusively to civilized races. Evidence strongly indicates that its great frequency in civilized man is in some way connected with his diet.

Appendicitis has been classified from various standpoints. The following classification has the advantage of simplicity and is probably as satisfactory as any: (1) acute catarrhal, (2) acute diffuse (including perforation and gangrene), (3) appendicular obstruction, and (4) chronic appendicitis.

Acute Catarrhal Appendicitis.—In acute catarrhal appendicitis the appendix is slightly swollen, the superficial vessels are engorged, and the mucosa is congested, swollen, and covered with mucus. Microscopically the inflammatory changes are confined primarily to the mucosa. Acute catarrhal appendicitis may pass into the diffuse form, heal with the production of characteristic scars that predispose to subsequent attacks, or undergo complete resolution.

Acute Diffuse Appendicitis.—This is the type of disease thought of when the term appendicitis is used without qualification. Here the appendix is greatly swollen, soft, and of a bright or dark red color; the serous surface may be covered with an inflammatory exudate; the mucosa may be ulcerated, and the lumen is filled with pus. There is a diffuse inflammation of all the layers of the wall of the appendix. When the inflammation is so intense as to cause a widespread suppuration of the walls of the appendix, the process is spoken of as *suppurative appendicitis*. When the inflammatory process reaches the serous surface of the appendix, there is set up a localized peritonitis which produces adhesions about the appendix that may later save the patient's life.

Perforation, which is most often due to necrosis from pressure exerted on the inflamed and weakened wall by a concretion in the lumen of the appendix, may occur at almost

any stage of the disease. It most often affects the tip of the appendix but may occur at any point. If the material in the lumen is under little or no tension and perforation takes place after adhesions have formed about the appendix, these adhesions may act as a wall which prevents the general dissemination of the infectious material, and a localized collection of pus limited by a wall of adhesions will be found surrounding the appendix. This is known as an *appendical abscess*. If the appendicitis is extremely acute and perforation takes place before adhesions have formed, or if the contents of the appendix are under such tension that the adhesions are broken when the perforation occurs, the infectious material is widely disseminated and a general peritonitis follows. Appendical abscesses usually enlarge and finally break into the general peritoneal cavity or evacuate their contents by establishing a fistulous opening into the intestine, but small abscesses may undergo absorption, leaving the appendix bound in a mass of adhesions.

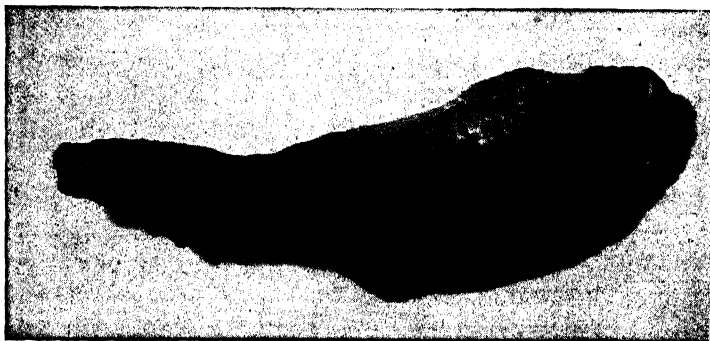


Fig. 185.—Acute diffuse appendicitis with gangrene. (From Anderson: Synopsis of Pathology.)

If, during the course of a diffuse appendicitis, the inflammation is so intense that there is an interference with the blood supply of the appendix by thrombosis of the vessels or by swelling, bending, or twisting of the appendix, gangrene results. The gangrene may be confined to the tip of the appendix, occur in multiple foci, or involve the whole organ. When gangrene occurs, perforation takes place, or the whole

appendix may slough off. Here the results of perforation are the same as those previously outlined.

Appendicular Obstruction.—Occasionally the lumen of the appendix becomes blocked by the sudden ingress of fecal material or by transitory swelling of the mucosa. The muscular contractions of the appendix in an effort to free itself of the obstruction give rise to sudden and intense pain, which will lead to the suspicion that the onset of a fulminating appendicitis is being dealt with if it is not borne in mind that disturbances of pulse rate and temperature occur in beginning appendicitis which is not the case in appendicular obstruction. If the appendix frees itself of the obstruction without injury to the mucosa no harm will be done; if the mucosa is injured acute appendicitis will most likely follow, and if the appendix is unable to free itself of the obstruction a series of changes analogous to those of acute intestinal obstruction follow. These changes however, are modified by the small size of the appendix and its peculiar histological structure and poor blood supply. It should be remembered that acute appendicular obstruction is often just as serious as acute appendicitis and calls for as immediate action. Fibrous stenosis and constriction of the appendix by bands, adhesions, folds, or kinking are important predisposing factors.

Chronic Appendicitis.—When a patient complains of vague abdominal pain, backache, flatulence, and slight tenderness over the appendix a diagnosis of chronic appendicitis is often made. That many of these patients have a true chronic appendicitis is most doubtful. A true chronic inflammation of the appendix is, to express it mildly, rare; but due to previous acute attacks the appendix may become thickened, constricted, kinked, and bound by adhesions to such an extent that it is predisposed to recurrent acute attacks and in rare instances the vague symptoms enumerated above may be produced.

In the condition known as *obliterative appendicitis* the appendix is shrunken, firm, and pale, and the lumen is completely or partially obliterated by an ingrowth of connective tissue. In some cases the obliterative process is confined to the end of the appendix. Appendicular obliteration may be

due to the atrophy of old age or it may be of inflammatory origin. Such appendices probably never give rise to symptoms in the absence of acute inflammation.

VII. THE RECTUM AND ANUS

A. Proctitis

Proctitis is inflammation of the rectum. It may be caused by bacterial infections, parasites, toxic agents, irritating injections, or irritation by fecal material, or it may be secondary to such conditions as hemorrhoids, rectal tumors, etc.

In acute proctitis the mucosa is swollen and edematous. Mucus, blood, and pus may be present. Ulceration may occur or the inflammation may extend through the rectal wall and involve the perirectal tissues producing a periproctitis.

B. Abscesses

The most important abscess connected with the rectum is the *ischiorectal abscess* which occurs in the loose tissue of the

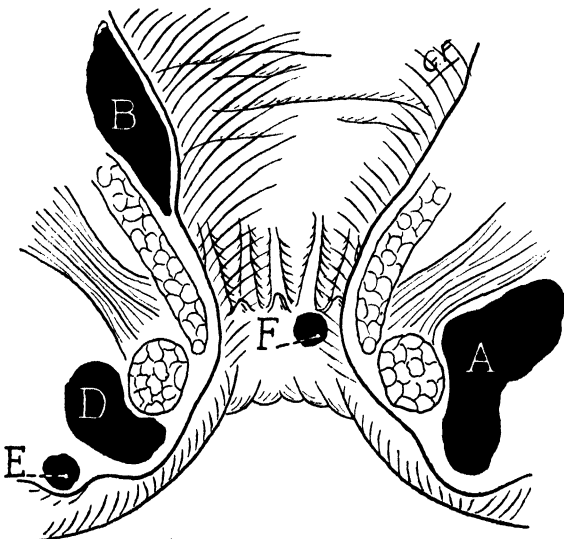


Fig. 186.—Abscesses of ano-rectal region. *A*, Ischiorectal abscess. *B*, Submucous or intramuscular rectal abscess. *D*, Subcutaneous abscess partially surrounding sphincter. *E*, Cutaneous abscess. *F*, Submucocutaneous or marginal abscess. (From Hirschman: *Ano-Rectal Diseases*, The C. V. Mosby Co.)

ischiorectal fossa and is due to the extension of an infection arising about the anal canal. An ischiorectal abscess may open into the rectum or both into the rectum and on the skin. The latter produces a fistulous tract connecting the lumen of the rectum with the outside of the body.

C. Fissure

An *anal fissure* is a painful linear ulcer which occupies one of the furrows between the longitudinal folds of the anal margin. They are due to traumatism or overstretching of the anal canal by the passage of hard fecal masses. The fissures become infected, and on account of repeated infection and overstretching fail to heal. They produce agonizing pain and may lead to pruritus ani and ischiorectal abscess.

D. Fistula

A *rectal fistula* is a discharging sinus or sinuses with one or more openings into the anal canal and one or more openings on the surface of the body or into some body cavity, such as

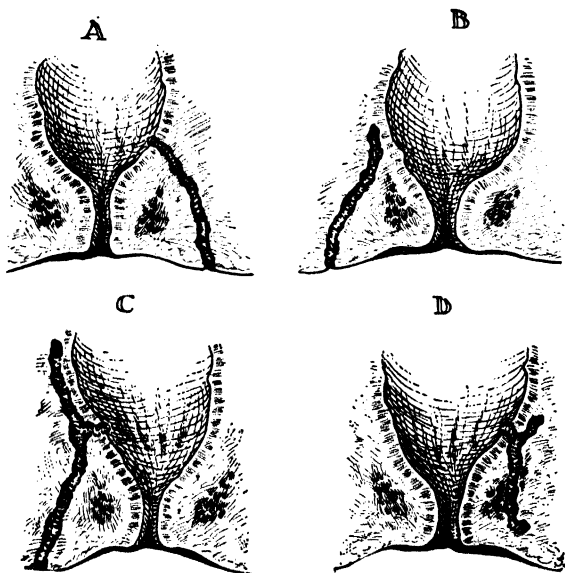


Fig. 137.—Rectal fistulas (fistula in ano). A, complete; B, blind external; C, fistula extending beyond point of opening into gut; D, blind internal. (From Hertzler and Chesky: *Surgery of a General Practice*.)

the vagina or bladder. They are usually formed in the following manner: the mucosa of the anus becomes infected and the infection burrows into the surrounding tissues, especially the ischiorectal fossa, leaving a fistulous tract behind it; an abscess develops and opens on the surface or into the vagina or bladder. When the tract reaches the surface or a body cavity, the fistula is said to be "complete"; until this has occurred, the fistula is said to be "incomplete."

E. Hemorrhoids

Hemorrhoids or *piles* are varicosities and dilatations of the veins that form a plexus beneath the lining of the rectum and anus. If the lower end of the plexus is affected the hemorrhoids are covered by the anal skin; if the upper end is affected they are covered by mucous membrane. Hemorrhoids that are covered by skin are known as "external" hemorrhoids; those that are covered by mucous membrane are known as "internal" hemorrhoids.

Any condition that interferes with the return of blood from the plexus or in any way throws an increased burden upon it predisposes to hemorrhoids. Among the general causes of hemorrhoids are failing heart action and cirrhosis of the liver with obstruction of the portal circulation. Among the local causes are constipation, pressure from a pelvic tumor or a pregnant or misplaced uterus, cancer of the rectum, enlarged prostate, etc. Constipation is by far the most important local cause.

Uncomplicated external hemorrhoids have the same appearance as varicose veins in other parts of the body. Internal hemorrhoids occur as elongated soft dark purple masses which arise from the first 3 or 4 cm. above the white line of Hilton* and hang down in the anal canal. In severe cases there are usually three large hemorrhoids with three small ones between them.

The slight oozing of blood which may accompany hemorrhoids is of importance on account of the extreme degree of anemia it may cause.

*The line that marks the junction of the rectal mucosa and the skin.

F. Benign Strictures of the Rectum

Benign strictures of the rectum may be congenital or acquired. Acquired strictures may be caused by external pressure from hands, adhesions, etc., or by narrowing of the lumen brought about by the contraction of scar tissue following inflammations, operations, etc. A common cause is lymphogranuloma inguinale. Benign strictures are usually located from an inch to one and a half inches above the anus. They are more common in Negroes than in white people.

G. Prolapse of the Rectum

Prolapse of the rectum is a pathological descent of one or more layers of the rectum through the anus. It occurs in two types: partial prolapse, in which the mucosa which descends normally through the anus during defecation fails to return to its normal position, and complete prolapse or procidentia, in which all layers of the rectum protrude through the anal canal.

H. Carcinoma of the Rectum

Carcinoma (cancer) of the rectum forms about 5 per cent of all cancers and about three-fourths of all intestinal tumors. It occurs more often in men than in women and is rare in Negroes. Certain rectal tumors which are usually considered benign, notably adenomas and papillomas, have a tendency to become cancerous.

Cancer of the rectum usually begins in the mucosa and gradually invades the muscular wall, producing a stricture. The most constant symptoms are bleeding, pain, and constipation or alternating diarrhea and constipation. The bleeding results from ulceration and the constipation results from stricture. Pain indicates that the growth has extended beyond the confines of the rectum because the rectum does not have any pain sensation. Probably the most constant early sign of cancer of the rectum is a feeling of discomfort in the rectum not relieved by defecation.

Cancer of the rectum may spread to the prostate, bladder, vagina, and uterus by direct extension; to the neighboring

muscles and lymph nodes by the lymphatic system, and to the liver by the blood stream. Death usually occurs in about two years.

VIII. THE LIVER

A. Degenerative Lesions

The liver is subject to practically all the degenerative lesions, such as cloudy swelling, amyloid infiltration, fatty changes, pigmentation, necrosis, etc.

Fatty Infiltration and Degeneration.—Fatty infiltration of the liver may be more or less physiological in children and in obese adults. In some cases the infiltration is due to overfeeding, while in other cases it is most likely due to a failure of the oxidation of fat. It is an accompaniment of prolonged alcoholism and tuberculosis, occurring in the latter regardless of whether the patient is obese or emaciated. In fatty infiltration the liver cells contain deposits of fat and the organ is enlarged, soft, and pale.

Prominent among the causes of fatty degeneration of the liver are passive hyperemia, certain anemias, phosphorus and certain metallic poisons, and certain intoxications and infections, especially pyemia and erysipelas. In fatty degeneration the liver is soft, reduced in size, and of a yellow color.

Acute Yellow Atrophy of the Liver.—The term “acute yellow atrophy” is applied to a condition which is not primarily a liver disease but a general cellular intoxication which falls most heavily on the liver. The term is a misnomer because the lesions are essentially necrotic instead of atrophic. Acute yellow atrophy of the liver is characterized by a primary enlargement followed by a marked reduction in the size of the liver, wrinkling of the capsule, jaundice, coma, and death. It occurs most often in young pregnant women but may occur in others as an accompaniment of smallpox, erysipelas, peritonitis, or syphilis. In pregnancy it may occur as a primary condition or it may follow eclampsia. Microscopically the liver presents a picture of complete degeneration affecting the parenchymatous cells.

B. Circulatory Disturbances

Portal Obstruction.—In portal obstruction there is an interference with the passage of blood through the portal vein to the liver. It may be due to thrombosis or pressure upon the vein outside the liver or its branches within the liver. When the portal vein becomes obstructed its tributaries dilate. Dilatation of the veins around the umbilicus leads to the formation of a “caput medusae” which is of characteristic appearance and diagnostic importance. Dilatation of the hemorrhoidal veins causes hemorrhoids, and fatal hemorrhage may result from varices formed in the esophagus and stomach. Ascites occurs and interferes with the emptying of the iliac veins, thereby causing anasarca of the lower limbs.

C. Infectious Hepatitis

Infectious hepatitis became a disease of importance during World War II. Its exact nature is not known but it appears to be caused by a virus or viruslike agent. It occurs in the presence of unsanitary conditions and often follows outbreaks of intestinal diseases. The exact mode of spread is not completely known. Transmission experiments indicate that one mode of spread is by the intestinal-oral route. The incubation period is from 18 to 30 days. The mortality is not high. Patients dying of the infectious hepatitis give a post-mortem picture very much like that of acute yellow atrophy of the liver. This disease was discussed on page 382.

D. Liver Abscess

Abscess of the liver may be caused by (1) extension of an inflammation from the gallbladder and bile ducts (biliary abscess), (2) the transfer of infectious material to the liver by the portal vein or hepatic artery (pyemic abscess), and (3) amebic dysentery.

Pyemic abscesses are most often secondary to ulcerative conditions of the intestine, purulent appendicitis, or suppurative hemorrhoids, but may occur as a part of a septic endocarditis or a generalized pyemia. Amebic abscesses are caused by *E. histolytica* carried from the intestinal ulcers of amebic dysentery to the liver by the portal vein.

Pyemic and biliary abscesses are often small and multiple. Amebic abscesses are usually single and often reach a large size. They are filled with a curdy, brown, foul-smelling material, which is partly pus and partly disintegrated liver cells.

A liver abscess may undergo absorption, become encapsulated and calcified, or rupture into the peritoneal or pleural cavity. Occasionally one opens on the outside of the body.

E. Cirrhosis of the Liver

Cirrhosis is a chronic affection of the liver characterized by an increase in the supporting connective tissue of the organ with degeneration of its parenchymatous cells. There are two main types of the disease: portal and biliary. In the former the changes occur around the branches of the portal vein; in the latter they occur around the bile ducts.

Portal Cirrhosis (Alcoholic Cirrhosis, Hobnail Liver).—This is the most common form of cirrhosis of the liver and is twice as common in males as in females. Alcohol, sedentary habits, and digestive disturbances are important etiological factors. Since the increase in connective tissue and destruction of parenchymatous cells is about the ramifications of the portal vein, portal obstruction with passive congestion of the abdominal viscera (of which splenic enlargement is an important sign), ascites, etc., are of constant occurrence in this type of cirrhosis. Since the bile ducts are not involved jaundice is rare. As a rule the liver is contracted, hard, and granular, and its surface is very irregular. Death ordinarily occurs within one to three years.

Biliary Cirrhosis (Hypertrophic Cirrhosis, Hanot's Cirrhosis).—In this type of cirrhosis the pathological changes occur around the bile capillaries instead of in the ramifications of the portal vein. Biliary cirrhosis may be caused by the irritation resulting from the stagnation of bile within the capillaries brought about by the closure of the bile ducts, by gallstones, tumors, etc. Another cause is infections of a general nature. Since the bile capillaries are primarily involved, jaundice is marked, and since the ramifications of the portal vein are not involved, there is no ascites or con-

gestion of the abdominal viscera. The liver is enlarged and its surface is smooth. As a rule death occurs within two or three years.

F. Tumors

Benign tumors of the liver are comparatively rare. Of these angiomas are most important because they may grow to a large size and rupture, with the production of a fatal hemorrhage.

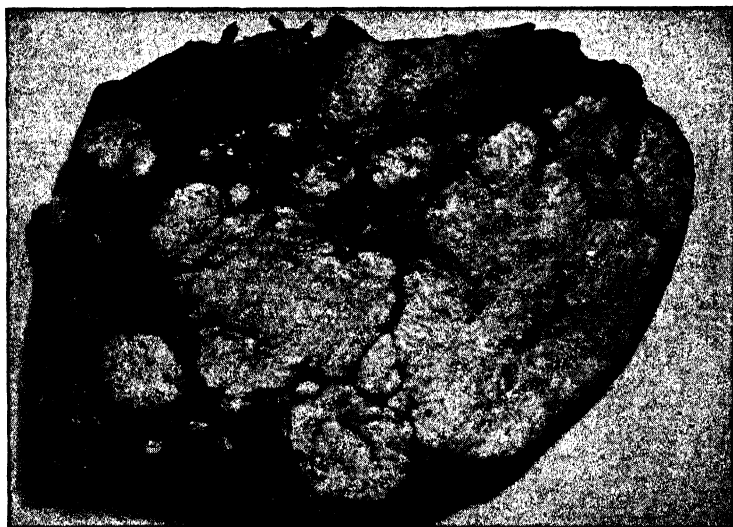


Fig 188.—Metastatic carcinoma in liver. (Primary tumor in the large intestine.) (From Anderson: *Synopsis of Pathology*.)

Of the malignant tumors carcinomas (cancers) and sarcomas are most important. Both ordinarily occur secondary to tumors in some other part of the body. Primary carcinomas and sarcomas are exceedingly rare.

IX. THE GALLBLADDER AND BILE DUCTS

A. Jaundice (Icterus)

The yellow color of blood plasma and bile is due to the bile pigment, bilirubin, which is derived from the hemoglobin liberated by the destruction of red blood cells and is excreted in the bile by the liver. If the liver loses its ability to

excrete the bilirubin normally formed or the destruction of red blood cells becomes so great that more bilirubin is formed than the liver can excrete, the pigment content of the blood rises to a high level and the tissues of the body undergo a yellow coloration, producing the condition known as *icterus* or *jaundice*. Icterus is characterized also by a slow heart rate, intense itching of the skin, prolonged clotting time of the blood, and a tendency to hemorrhage. In many cases bile appears in the urine and other excretions.

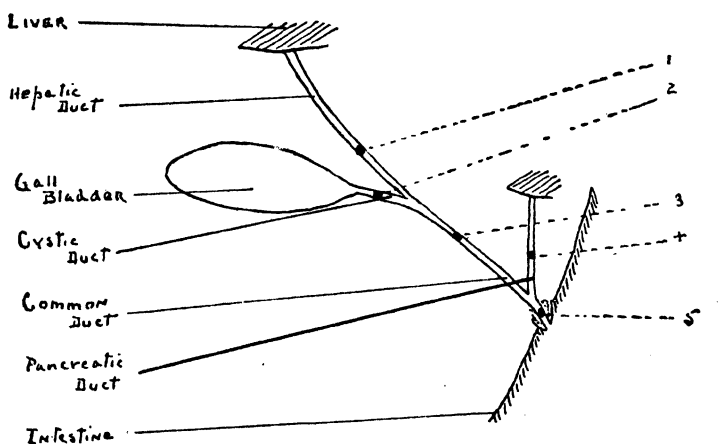


Fig. 189.—This is a schematic sketch to illustrate the arrangement of the bile passages and the effects of lesions in them. Bile formed in the liver is stored in the gallbladder from which, as occasion demands, it passes into the small intestine. An obstruction in the cystic duct does two things; it prevents the storage of bile, and it prevents what bile happens to be in the gallbladder from reaching the intestine. No clinical symptoms follow either of these eventualities. On the other hand, an obstruction in either the hepatic duct or the common duct prevents the bile from reaching the intestine and jaundice (icterus) results. Blocking of the pancreatic duct hinders the pancreatic secretion from entering the intestine. If an obstruction occurs in the common duct below the entrance of the pancreatic duct, bile may be forced into the latter and cause pancreatic disease. (From Woolley: *Fundamentals of Pathology*.)

Jaundice due to interference with the excretion of bile by the liver is known as *obstructive* or *hepatogenous* jaundice, and jaundice due to an overproduction of bilirubin is known as *hematogenous* jaundice. The most important causes of obstructive jaundice are inflammations that cause swelling of the mucosa and occlusion of the excretory bile ducts (catarrhal jaundice), foreign bodies such as gallstones in the excretory bile ducts, outside pressure on the excretory bile

ducts or occlusion of the bile ducts within the liver by cirrhosis, etc. If occlusion affects only the cystic duct, jaundice will not occur. Among the important causes of hematogenous jaundice are those diseases characterized by an increased destruction of red blood cells, such as certain anemias, severe infections, certain poisons, and the disease entity known as hemolytic jaundice. Weil's disease, or epidemic jaundice, is caused by the *Spirochaeta icterohaemorrhagiae*.

A type of jaundice which became rather important during World War II is known as *homologous serum jaundice*. It follows the parenteral injection of the whole blood, plasma, or serum of a person whose body harbors the causative agent. The reason that it became important in World War II was that it often followed the injection of vaccine to prevent yellow fever (human serum is used in the preparation of one type of yellow fever vaccine). The causative agent of homologous serum jaundice appears to be viruslike in its nature and is apparently related to the causative agent or infectious hepatitis. Homologous serum jaundice was previously discussed on page 382.

The prolonged clotting time of the blood and the tendency to hemorrhage cause operations on patients with jaundice to be attended with great danger, and this is especially true if the jaundice has existed for a long time.

B. Inflammations

Inflammation of the bile ducts is known as *cholangitis*; inflammation of the gallbladder is known as *cholecystitis*. Both may be acute or chronic.

Acute Cholecystitis.—Acute cholecystitis may be catarrhal or suppurative and may have its beginning in the gallbladder as a result of the irritation caused by gallstones or retained bile, or it may represent the extension of a cholangitis. Suppuration may be so extensive that the gallbladder becomes filled with a purulent exudate (*empyema of the gallbladder*), and peritonitis may occur on account of rupture of the gallbladder or direct extension of the infection through its wall. The danger of extension of the infection and the severity of the symptoms make suppurative cholecystitis a surgical emergency.

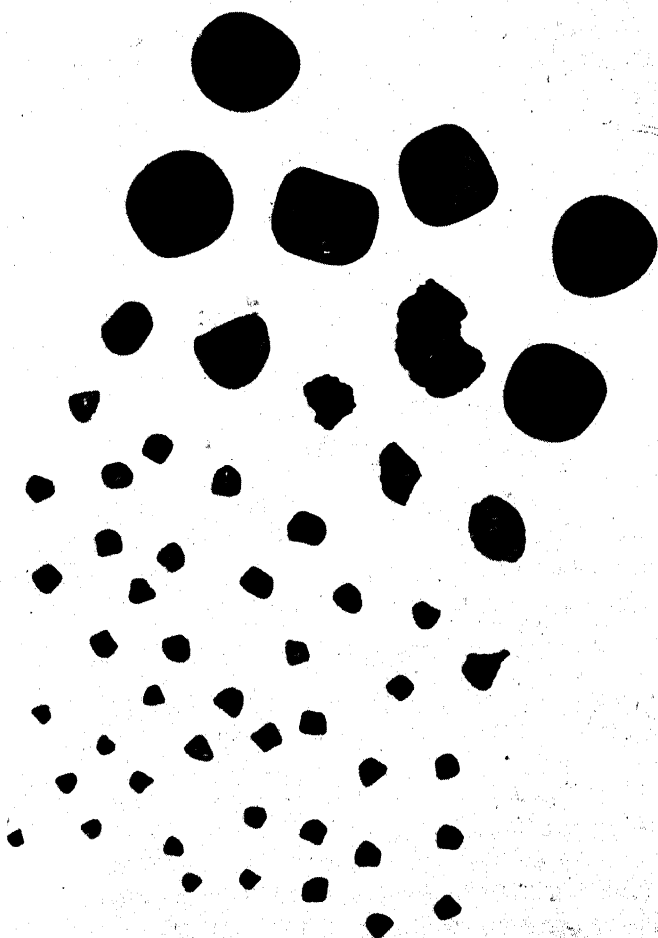


Fig. 190.—Gallstones. Note the variation in size and shape.

Chronic Cholecystitis.—Chronic cholecystitis may follow the acute form or be chronic from the beginning. Many cases follow typhoid fever. The condition of the gallbladder depends on the relation existing between infection and obstruction. If infection forms the principal feature and obstruction is slight, the wall is thickened, elasticity is lost, and the size of the cavity is reduced. If infection plays an insignificant part and obstruction plays the major rôle, the wall is thin and the organ is markedly dilated and filled with a viscid fluid.



Fig. 191.—Cholecystitis and cholelithiasis. Note the multiple faceted calculi. (From Anderson: Synopsis of Pathology.)

Chronic cholecystitis is of importance in the production of gallstones, and gallbladders containing stones are often the site of acute or chronic cholecystitis.

C. Gallstones

Gallstones are concretions which ordinarily form in the gallbladder but may form in the larger bile ducts and are composed of certain solid constituents of the bile which have undergone precipitation. They often have a nucleus of bacteria and a framework of dead cells derived from the epithe-

lumen of the gallbladder or duct in which they are situated. In some cases the nucleus is composed of inspissated mucus or devitalized cells.

The causes of gallstones are those conditions that bring about a precipitation of the solid constituents of the bile. Important among these are inflammation of the gallbladder or bile ducts, obstruction to the outflow of bile, and an increase in the cholesterol content of the blood. Of these, inflammation is most important. Gallstones frequently follow typhoid fever, in which two important etiological factors (infection and increased cholesterol content of the blood) are present. In such cases typhoid bacilli form the nuclei of the stones. Other bacteria that have been found in the nuclei of gallstones are colon bacilli, streptococci, and staphylococci.

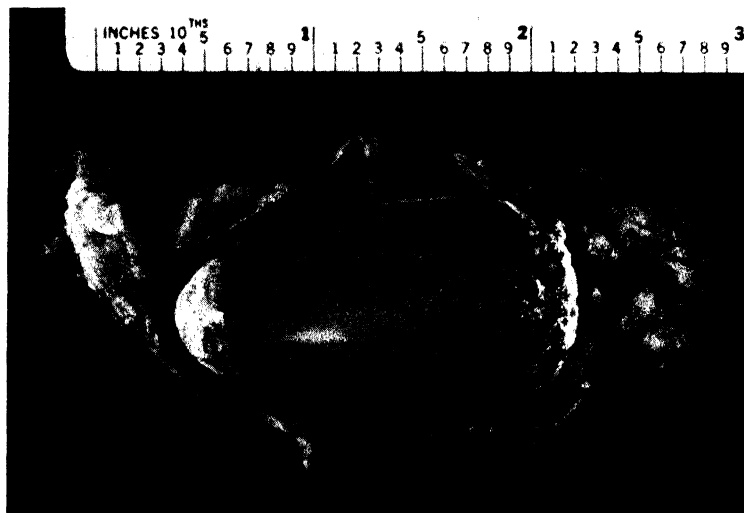


Fig. 192.—Dissection showing a large stone in gall bladder.

Gallstones may be single or multiple. In multiple stones the number may run into the hundreds. Single stones are usually round or oval. Multiple stones are usually faceted. Gallstones may be composed of cholesterol, calcium bilirubin, or combinations of the two (mixed stones). Cholesterol stones are large, single, oval, comparatively smooth, and seldom

cause symptoms. Typhoid fever and pregnancy predispose to this type of stone. Mixed stones (the most common type) are usually multiple and are composed of concentric layers of cholesterol and bile salts. Calcium bilirubin stones are small, black, and granular in appearance.

Stones may exist for many years without causing symptoms other than vague abdominal distress, and this is especially true of the larger smooth stones because they do not enter the bile passages and do not cause so much irritation as stones with a rough surface. If a stone attempts to leave the gallbladder or enter a duct, an attack of gallstone colic is brought about. The attack usually terminates suddenly when the stone passes through the duct or drops back into the gallbladder, and terminates gradually when the stone becomes impacted in a duct. When a gallstone becomes lodged in the common duct, the patient becomes jaundiced and the stools become clay colored on account of their high fat content. If a stone is in the cystic duct, jaundice does not occur unless the end of the stone obstructs the common duct, but bile is kept from entering the gallbladder and the gallbladder may become shriveled and thickened or thin and distended with mucus. The latter is known as *hydrops* of the gallbladder. If infection occurs empyema of the gallbladder is produced. Gallstones may cause ulceration and perforation of the wall of the gallbladder.

X. THE PANCREAS

A. Fat Necrosis

When the pancreas is injured to such an extent that the pancreatic juice escapes, the fatty tissue with which the juice comes in contact undergoes a peculiar type of digestion known as fat necrosis. The digestion is due to the action of the pancreatic lipase on the fat cells. The fatty tissue most often affected is that of the pancreas itself, the omentum, and the mesentery. The causes of fat necrosis are those conditions that bring about destructive lesions of the pancreatic tissue, important among which are acute and chronic pancreatitis, obstruction of the pancreatic duct, and tumors.

B. Pancreatitis

Pancreatitis may be acute or chronic, and the acute type may be hemorrhagic or suppurative. The source of infection may be the bile passages, the duodenum, or the surrounding tissues. Infection from the bile passages is brought about by the blocking of the ampulla of Vater by a stone or other means which obstructs the passage of the bile into the duodenum and causes it to back up into the pancreatic duct. Infections of neighboring organs may spread directly to the pancreas. Pancreatitis often leads to jaundice and fat necrosis.

C. Relation of the Pancreas to Diabetes Mellitus

(See page 747.)

XI. THE PERITONEUM

A. Ascites

By *ascites* is meant the accumulation of a serous exudate in the abdominal cavity. It may occur as a part of a general dropsy brought about by failing heart action or impaired kidney function, but the most pronounced cases are caused by portal obstruction, especially when the obstruction is due to cirrhosis of the liver.

The collection of ascitic fluid in the abdominal cavity displaces the abdominal organs and embarrasses respiration by making upward pressure on the diaphragm. Pressure on the veins may lead to passive congestion of the lower extremities.

B. Peritonitis

Peritonitis is inflammation of the peritoneum. It is usually acute but may be chronic. It occurs most often as a localized process but may become generalized. The most common type of chronic peritonitis is tuberculous peritonitis. On the other hand, tuberculous peritonitis may develop with such rapidity as to give rise to acute symptoms.

1. ACUTE PERITONITIS

Acute peritonitis may occur as a result of mechanical irritation (as occurs when the peritoneum is unduly trauma-

tized during operations or when sterile foreign bodies, such as sponges, are left in the peritoneal cavity) or of chemical injury (as occurs when antiseptics are applied to the peritoneum), but most cases are due to bacterial infection, and the bacteria most often responsible are *Bact. coli*, streptococci, staphylococci, and pneumococci.

Bacteria may reach the peritoneal cavity (1) through perforations in the walls of abdominal viscera, (2) by passing directly through the gangrenous wall of an abdominal viscus, (3) by extending through a fallopian tube, (4) from the outside by way of accidental or surgical wounds, and (5) by the blood stream. The last method is infrequent, but it may occur in general septicemia.

Ordinarily acute peritonitis begins as a local condition and in the majority of cases remains localized on account of the prompt formation of adhesion about the site of infection, but in some cases the infection spreads rapidly and brings about a general peritonitis.

If a localized peritonitis does not spread rapidly and produce a general peritonitis, it undergoes resolution or abscess formation. Peritonitis caused by the rupture of a gastric, duodenal, or typhoid ulcer and peritonitis due to streptococci or pneumococci rapidly become generalized and quickly cause the death of the patient.

In general peritonitis the process may be either septic or suppurative. In the septic type death occurs from absorption of toxins before any marked peritoneal changes have taken place. In the suppurative type suppuration and marked peritoneal change occur.

Peritonitis due to *Bact. coli* is the most common form and, fortunately, is often comparatively benign. The organisms reach the peritoneum from the intestinal tract which happens most often as a complication of appendicitis. Streptococcus peritonitis usually results from penetrating wounds of the abdomen or an extension of a puerperal sepsis. Pneumococcus peritonitis may occur secondary to a pneumococcus infection in some other part of the body or as a primary condition. In primary pneumococcus peritonitis the organisms reach the peritoneum through the vagina, uterus, and fallopian tubes.

2. TUBERCULOUS PERITONITIS

Tuberculous peritonitis is most common in children and young adults. It ordinarily occurs secondary to tuberculosis in some other part of the body. It may occur rather acutely as a part of a generalized miliary tuberculosis or as a chronic process which is most often secondary to tuberculosis of the fallopian tubes, ovaries, or mesenteric lymph nodes. Less often it is secondary to tuberculosis in far distant foci. The symptoms of general miliary tuberculosis may be so prominent that the abdominal symptoms are entirely overlooked or an erroneous diagnosis of typhoid fever may be made in which case the abdominal symptoms are attributed to the typhoid infection.

The chronic form may be moist or dry. In the former the peritoneum is studded with small tubercles and a voluminous thin yellow exudate is present; in the latter the coils of intestines are matted together by adhesions and the omentum is greatly thickened. Tubercles may or may not be present.

With modern methods of treatment, tuberculous peritonitis is not as hopeless as it once was, and this is especially true when the primary focus of infection, such as an ovary or fallopian tube, can be found and removed.

C. Abdominal Adhesions

The contraction of abdominal adhesions may lead to conditions varying from mild discomfort to intestinal obstruction.

D. Tumors of the Peritoneum and Neighboring Structures

The most important tumor of the peritoneum is the metastatic carcinoma originating in other abdominal organs. The stomach is the most common site of the primary growth and the ovary is next. Peritoneal cancer is frequently accompanied by ascites and hemorrhage.

A peculiar tumor growth of the peritoneum is *pseudomyxoma peritonei* which follows ruptures of pseudomucinous cysts of the ovary or less frequently mucous cysts of the appendix. In this condition the peritoneum becomes covered with masses of gelatinous material that is so soft that it may

be scraped away. These masses may occur in every part of the abdominal cavity and cause extreme distention. In a few cases removal of the primary growth checks the peritoneal spread, but as a rule the disease proves fatal.

Questions for Review

1. What is the most common site of extragenital chancres?
2. Discuss cancer of the lip.
3. Give some of the causes of retropharyngeal abscess.
4. What are some of the causes of gastric hemorrhage? How may it be determined whether blood came from the stomach or lungs?
5. Give the symptoms experienced in hemorrhage from a peptic ulcer.
6. What is the composition of gastric contents during digestion?
7. What are the two methods of examining gastric contents?
8. In gastric analysis what is meant by free hydrochloric acid? Combined acid? Total acidity?
9. Of what significance is the presence of free hydrochloric acid in the gastric contents?
10. Give the characteristics of the gastric contents in cancer of the stomach and ulcer of the stomach.
11. What is Meckel's diverticulum? What is its origin? Why is it important?
12. What is a hernia? Name the different kinds and discuss each kind.
13. What are the following kinds of hernia: reducible, obstructed, strangulated?
14. What is the difference between mechanical and paralytic obstruction of the intestine?
15. Define: intussusception, volvulus.
16. Give the life cycle of a tapeworm.
17. Briefly discuss appendicitis.
18. How is an anal fistula formed?
19. Give the kinds and some of the causes of hemorrhoids.
20. What is the most common sign of cancer of the rectum?
21. Give some of the causes and some of the symptoms of portal obstruction.
22. Discuss jaundice—its origin and significance.
23. What is the origin of gallstones?
24. How may bacteria reach the peritoneum?
25. Discuss tuberculous peritonitis.

True-False Test

Place the word "true" or "false" before each statement.

- 1. Stomatitis, glossitis, and gingivitis are closely related.
- 2. Cancer of the stomach is more common in men than in women and usually affects the pyloric end of the stomach.

- 3. Under normal conditions the stomach secretes two or three quarts of gastric juice daily.
- 4. Strong emotions inhibit the flow of gastric juice.
- 5. Pepsin is an enzyme, found in gastric juice, which aids in the digestion of proteins.
- 6. In gastric ulcer there is usually a deficiency in hydrochloric acid.
- 7. The presence of large amounts of lactic acid in the stomach suggests cancer of the stomach.
- 8. In cancer of the stomach, pernicious anemia, and pellagra, there is an increase in the amount of free hydrochloric acid in the stomach.

Completion Test

- 1. -----tonsillitis gives rise to the greatest enlargement of the tonsils.
- 2. ----- is the most important congenital defect of the stomach.
- 3. Among the local effects of cancer of the stomach are -----, ----- and -----.
- 4. ----- and ----- assumed considerable importance during World War II.

References

- Boyd, William: Surgical Pathology, Philadelphia, 1947, W. B. Saunders Co.
- Mead, Sterling V.: Diseases of the Mouth, St. Louis, 1940, The C. V. Mosby Co.
- Eusterman and Balfour: The Stomach and Duodenum, Philadelphia, 1935, W. B. Saunders Co.
- Hirschman, Louis J.: Synopsis of Ano-Rectal Diseases, St. Louis, 1942, The C. V. Mosby Co.
- Craig and Faust: Clinical Parasitology, Philadelphia, 1945, Lea & Febiger.
- Gradwohl, R. B. H.: Clinical Laboratory Methods and Diagnosis, St. Louis, 1948, The C. V. Mosby Co.
- Anderson, W. A. D.: Synopsis of Pathology, St. Louis, 1946, The C. V. Mosby Company.
- Kantor, John L.: Synopsis of Digestive Diseases, St. Louis, 1937, The C. V. Mosby Co.
- Paul, J. R.: Infectious Hepatitis, Bull. New York Acad. Med. 22: 204-216, (April) 1946.

CHAPTER LV

DISEASES OF THE URINARY SYSTEM

I. THE KIDNEYS

A. Renal Hemorrhage

The three important causes of massive renal hemorrhage are tumors, tuberculosis, and stones.

B. Nephritis

The term *nephritis* or Bright's disease is applied to conditions that affect both kidneys diffusely and are due to inflammation or degenerative changes of the kidneys or diseases of their blood vessels. The important feature of nephritis is its diffuse bilateral nature which distinguishes it from localized affections of the kidneys, such as abscesses, etc. The inflammations causing nephritis are nonsuppurative. Depending on its varied etiology, pathology, and symptoms, there are many forms of nephritis, and from these standpoints most elaborate classifications of the disease have been proposed. Unfortunately, no classification is entirely satisfactory. A classification which was formerly much used and for which there is some justification is (1) glomerulonephritis in which the glomeruli are primarily involved, (2) tubular nephritis in which the tubules are primarily involved, and (3) interstitial nephritis in which the interstitial tissue is primarily involved. This classification like most others is weakened by the fact that the disease seldom occurs in pure form; i.e., although one component of the kidney is primarily attacked all are more or less involved. The more recent classifications indicate the degenerative condition of the kidneys by the term *nephrosis* and reserve the term "nephritis" for the true inflammatory condition. If this classification is followed, the lesions of nephrosis will be found primarily in the kidney tubules, while true nephritic lesions will be found to affect the glomeruli or interstitial tissue.

In the majority of cases nephritis is due to irritants brought to the kidneys by the blood stream. These irritants

may be bacteria or their products, chemical poisons, or certain poisonous products that arise within the body.

When the kidneys become diseased, they often lose their ability to concentrate nitrogenous waste products (uric acid, urea, and creatinine), chlorides, and other substances which have been brought to them by the blood stream for excretion and these waste products accumulate in the blood. Along with the loss of their power to excrete waste products the kidneys lose their ability to excrete certain inert dyes, such as phenolsulphonaphthalein, used for the purpose of testing kidney function. On account of the increased permeability of the glomeruli, serum albumin escapes from the blood into the urine.

When the tubules of the kidneys become diseased, albuminous material collects in them and coagulates, forming molds or *casts* of the tubules. The pressure of the fluid behind the casts sweeps them out of the tubules with the urine. The material of which the casts are composed may pass from the blood through the diseased glomeruli and tubules, or it may be derived from the degeneration of the epithelium of the tubules. Casts made up of this coagulated material alone are known as *hyaline* casts and are the least significant of all. Granules, pus cells, red blood cells, or epithelial cells may become incorporated in the casts giving rise to granular, pus, blood, and epithelial casts respectively. Granular casts indicate a comparatively mild degeneration of the tubules and epithelial casts indicate a more severe degeneration. Blood and pus casts respectively, indicate hemorrhage and suppuration of one or both kidneys.

High blood pressure due to changes in the minute arterioles of the kidneys is a frequent accompaniment of nephritis. Many cases of nephritis are accompanied by a more or less extensive edema which may be due to the changes in the kidneys themselves or to cardiac failure brought about by the high blood pressure.

As a rule cases of nephritis in which the glomeruli are primarily involved are characterized by high blood pressure, retention of nitrogenous waste products, and a tendency to uremia, while tubular nephritis is characterized by little or

no increase in blood pressure, no retention of nitrogenous waste products, and little tendency to uremia.

Acute cases of nephritis may recover without leaving any marked alteration of the kidneys, heal with scar formation, become chronic, or cause immediate death. Death in acute nephritis may result from cardiac failure or cerebral hemorrhage, both of which are caused by high blood pressure, or it may be due to uremia which will be discussed at a later time. In chronic nephritis death may be due to any of those conditions that cause death in acute nephritis or it may be brought about by intercurrent infection.

C. Uremia

The term "uremia" indicates a condition, the cause of which is not known, that often enacts the terminal scene in both acute and chronic nephritis. The symptoms most often manifested are headache, convulsions, drowsiness and stupor, deepening into a coma that ends in death. In other cases nausea, vomiting, and diarrhea are prominent features. It was once thought that the symptoms of uremia were due to the accumulation of urea in the blood. This is now known to be untrue. It is probably not due to vascular disturbances or many things that have been mentioned as etiological factors.

D. Tuberculosis of the Kidney

Tuberculosis of the kidney may occur rather acutely as a part of a generalized miliary tuberculosis or as a chronic local condition. The first type is not of great importance and will not be discussed here.

Chronic tuberculosis of the kidney is most often secondary to tuberculosis of the lungs, bones, or lymph nodes, and the bacilli reach the kidney by way of the blood stream.

Chronic renal tuberculosis begins as one or more tubercles, and as the condition progresses the tubercles are converted into cheesy foci that undergo liquefaction and discharge their contents into the renal pelvis, leaving the kidney more or less honeycombed with cavities which may continue to enlarge and coalesce until all that remains of the kidney is a shell surrounding multiple cavities. In the beginning chronic

renal tuberculosis is unilateral, but after a time the other kidney becomes involved. As a rule, the urine shows blood, pus, and tubercle bacilli.

E. Tumors of the Kidney

While various benign and malignant tumors may occur in the kidneys, the only ones of sufficient importance to be discussed here are the hypernephromas and mixed tumors of the kidney. Both are malignant.

Hypernephroma.—The name hypernephroma was given to a group of tumors that were formerly thought to arise from remnants of adrenal tissue that had been included in the kidney during embryonic development, but it is now known that these tumors arise from the kidney itself. However, the term hypernephroma has become so well established that it will probably be used for many years to come.

Hypernephromas occur as yellowish, greasy masses that often show areas of hemorrhage and small cysts. They may be small and remain so throughout their course, or they may suddenly begin to grow rapidly and quickly form bulky tumors that destroy the kidney substance and extend to the kidney pelvis, renal veins, and vena cava. On the other hand, apparently quiescent tumors may give rise to fatal metastases. Metastasis occurs most often to the lungs, bones, and the opposite kidney. About 20 per cent of hypernephromas have already metastasized when first observed by the physician. The most common early symptom is hematuria. They occasionally give rise to a long-continued fever, and this is always to be thought of when a prolonged unexplained fever occurs.

The removal of the involved kidney before metastasis occurs will effect a cure unless there is a tumor in the other kidney, which is sometimes the case. Most hypernephromas occur in persons more than 45 years of age. They probably never occur in children.

Congenital Mixed Tumors (Teratomas).—These tumors are of congenital origin and usually show clinical manifestations before the third year of life. They are composed of muscle fibers, cartilage, bone and fatty tissue. They often grow rapidly and to a large size, but metastasis is infre-

quent and occurs late. Death is most often due to intra-abdominal extension. There is no hopeful method of treatment. A kidney tumor occurring after the seventh year is more likely to be a hypernephroma than a congenital mixed tumor.



Fig. 193.—Hypernephroma. Tumor located at the upper pole of the kidney.

II. THE KIDNEY PELVIS AND URETERS

A. Pyelitis

Pyelitis, or inflammation of the kidney pelvis, occurs most often in childhood, during pregnancy, or as a complication of kidney stones.

The organisms most often responsible for pyelitis are *Bact. coli*, staphylococci, and streptococci. They may reach the

kidney by the blood stream or by ascent from an inflammatory condition of the lower urinary tract. Pyelitis is usually bilateral, but the right kidney often shows greater involvement than the left.

B. Hydronephrosis

Hydronephrosis is a dilatation and filling with urine of the kidney pelvis and ureter, with atrophy of the kidney tissue, brought about by an obstruction to the outflow of urine. Obstruction of both ureters, the urethra, or bladder, causes a bilateral hydronephrosis while an obstruction of one ureter causes a unilateral hydronephrosis. Obstruction of a ureter may be due to congenital atresia, strictures, kinks, impaction of stones, or outside pressure from tumors. Obstruction in the bladder may be due to stones, tumors, or diseases of the spinal cord that cause paralysis of the bladder muscles. Obstruction of the urethra may be caused by strictures, prostatic enlargement, or congenital malformations. A bilateral hydronephrosis of sufficient degree is incompatible with life.

C. Pyonephrosis

In *pyonephrosis* there is a dilatation of the kidney pelvis and ureter as is the case in hydronephrosis, but they are filled with pus instead of urine. Pyonephrosis may be due to tuberculosis, infection around a calculus, or infection of a hydronephrosis. The pus is thick, and often there is so much destruction of tissue that the kidney is converted into a thin-walled sac filled with purulent material.

D. Renal Calculi

(Kidney Stones, Nephrolithiasis)

Renal calculi are formed in the kidney pelvis by the precipitation of normal or abnormal constituents of the urine. They may be large or small and sandlike, smooth or rough, and of a regular or irregular contour. They are usually single but may be multiple. As a rule, the larger calculi form more or less complete casts of the kidney pelvis and have projections that extend between the calices of the kidney. These are known as dendritic or coralliform stones, and in some cases

the branching may be so extensive as to remind one of the antlers of a deer. Kidney stones often enter the ureter where they may become arrested or pass to the bladder.

Just why renal calculi are formed is not known, but there are certain factors which act as predisposing causes. Among them are infection of the kidney pelvis, interference with the outflow of urine, and certain other factors not well understood.

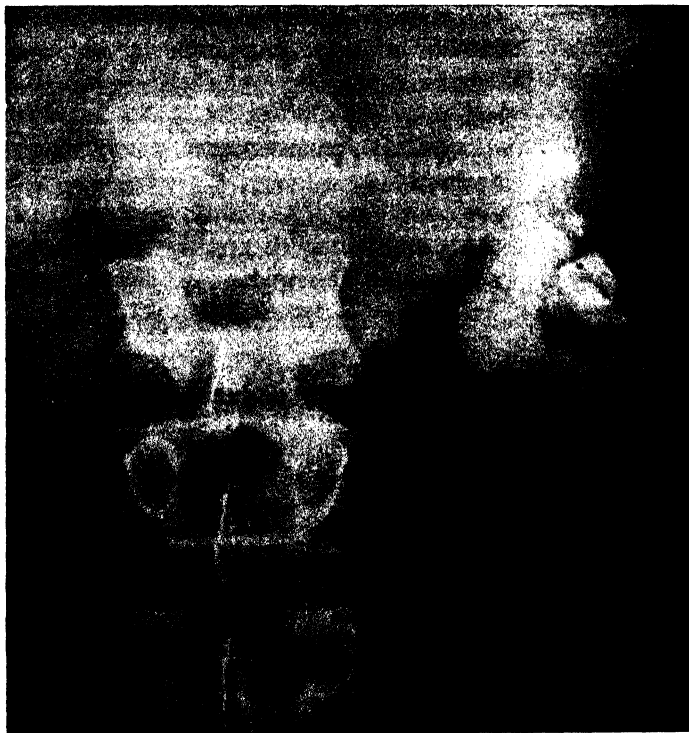


Fig. 194.—X-ray picture showing a renal calculus. The stone is in the left kidney. (From Meakins: *The Practice of Medicine*.)

The symptoms of renal calculi show marked variation depending on the size and shape of the calculus and the presence or absence of a complicating infection. If the kidney pelvis is not infected and the stone is smooth and not small enough to enter the ureter, symptoms will be slight or absent.

If a stone enters the ureter, it brings on an attack of renal colic. In most cases the stone passes on to the bladder. If it is arrested in the ureter hydronephrosis develops unless the stone is surgically removed. Ulceration and stricture formation often occur at the point of lodgment. Large irregular stones of the kidney pelvis may cause extensive ulceration and destruction of tissue. Stones in any location strongly predispose to infection; therefore, pyelitis is a common complication of kidney stones, and a hydronephrosis following the impaction of a stone in the ureter is often converted into a pyonephrosis.

III. THE BLADDER

A. Cystitis

The healthy bladder is remarkably resistant to infection, but a bladder weakened by injury or disease is as liable to infection as any other organ. The conditions which weaken the bladder and predispose to cystitis are obstruction to the outflow of urine, paralysis of the bladder muscles, vesical calculi, and tumors. Like most other inflammatory conditions cystitis may be acute or chronic.

While cystitis may be brought about by the excretion of highly concentrated urine or irritating drugs, it is almost always due to bacterial infection, and the bacteria most often responsible are *Bact. coli*, staphylococci, streptococci, *E. typhosa*, and gonococci. As a rule, the cocci have a tendency to cause an acute cystitis, while infections due to bacilli assume a more chronic form. In streptococcus and staphylococcus infections, the organisms render the urine alkaline, while in cystitis due to the colon bacillus, typhoid bacillus, and gonococcus, the urine is acid. A cystitis accompanied by alkaline urine is usually more severe than one accompanied by acid urine.

The causative organisms may reach the bladder by way of the urethra or they may descend from the kidney pelvis and ureter, and in a few cases they are brought to the bladder by the blood or lymph stream. They may reach the bladder from the urethra by the extension of a posterior urethritis or they may be introduced through the urethra by the use of

dirty instruments. When the infection descends from the renal pelvis, regression of the cystitis often follows the cure of the primary condition.

In acute cystitis all the signs of an active inflammation are present. The urine contains the causative organisms, many degenerated bladder cells, mucus, and pus. Hemorrhage may be present. In some cases the bladder wall may become so soft that it is easily penetrated by a catheter.

Chronic cystitis follows acute cystitis or occurs as a primary process. Some degree of chronic cystitis practically always accompanies vesical calculi. As a rule, the bladder wall is thickened and in some cases the mucosa may show polypoid outgrowths, or portions of its transitional epithelium may be converted into stratified squamous epithelium.

B. Vesical Calculi

(Bladder Stones)

Vesical calculi may occur in the form of fine particles or as stones of considerable size. They are formed from constituents of the urine which ordinarily remain in solution but have undergone precipitation on account of supersaturation or other changes in the urine. The constituents of the stone are deposited on a nucleus which may be a stone that has descended from the kidney pelvis, a foreign body, or a clump composed of epithelial cells, mucus, and pus or bacteria, although such a nucleus is often not discernible. Vesical calculi often follow catarrhal conditions of the bladder or stagnation of urine.

Vesical calculi are usually single and spherical but may be multiple and faceted. They promote inflammation and may cause ulceration and perforation of the bladder wall. If the stone becomes engaged in the urethra, the patient is seized with a paroxysm of pain and hemorrhage which is spoken of by the laity as "an attack of gravel."

C. Tumors

The most common tumor of the bladder is the papilloma which appears as a soft shaggy tumor growing from the bladder wall. It is most common in men between thirty and

fifty years of age. A painless hematuria is the chief symptom. On account of their tendency to become malignant all tumors of the bladder should be considered malignant until proved innocent.

IV. THE URETHRA

A. Urethritis

Urethritis is of two types: specific due to gonococci and nonspecific due to other causes. The former is much more common. Both types may be either acute or chronic.

Nonspecific Urethritis.—Nonspecific urethritis may be caused by highly irritating injections or bacteria introduced by nonsterile instruments. The organisms most often responsible for this form of urethritis are staphylococci and streptococci. A nonspecific urethritis may accompany such infections as scarlet fever and smallpox, and in the female a nonspecific infection of the vulva and vagina may spread to the urethra.

Gonorrheal Urethritis.—Gonorrheal urethritis begins in the male as an anterior urethritis and with proper care remains limited to that portion of the urethra but when improperly treated extends to the posterior urethra. When the posterior urethra becomes infected, the condition becomes more serious on account of infection of the various crypts and glands connected with the posterior urethra and the likelihood of the further spread of the infection to the prostate, bladder, epididymis, and seminal vesicles. The posterior urethra may also act as a focus of infection from which gonococci are spread to the joints. An intractable chronic infection of the glands connected with the urethra is likely to persist long after the acute infection has subsided, and the inflammatory changes in the urethra are likely to lead to stricture formation.

In the female, gonorrhea primarily attacks the urethra and cervix. From the cervix the organisms pass through the uterine cavity, which is little affected, to the fallopian tubes, with the production of a salpingitis that is often complicated by a localized peritonitis.

The important complications of gonorrheal urethritis, other than extension to the organs previously mentioned, are abscess of the periurethral glands (periurethral abscess) in both sexes, stricture of the male urethra and abscess of Bartholin's glands in the female. In both male and female the glands connected with the urethra may act as important harboring places for gonococci. Gonorrhea has previously been discussed on page 328.

B. Stricture

Stricture of the urethra results from the contraction of scar tissue that has formed within the urethral wall. Stricture may be of congenital or traumatic origin, but the great majority occur as an aftermath of gonorrhea. As a rule strictures develop slowly, and signs of obstruction may not appear until long after the condition that caused the stricture has subsided. Stricture of the urethra is not common in women.

When the obstruction becomes far advanced, the urethra dilates behind the stricture, and this is followed by hypertrophy and dilatation of the bladder with bilateral hydro-nephrosis. Ulceration behind the stricture or perforation by the false passage of sounds may lead to an extravasation of urine, involving the external genitalia, perineum, and the skin of the thighs and lower abdomen.

C. Urethral Caruncle

A urethral caruncle is a peculiar growth of very vascular granulation tissue that arises within or near the orifice of the female urethra. Usually, it is single, sessile, or pedunculated, of a bright red color, and extremely tender. They have a tendency to occur in elderly women and are troublesome on account of the pain which they cause, especially on urination.

V. URINE

A. General Characteristics

Urine is essentially an aqueous solution of waste products. Its constituents may be classified as those which are normally excreted, and those which appear in the urine as a result

of disease. In the first group are uric acid, urea, creatinine, chlorides, sulphates, and phosphates. In the second are sugar, albumin, bile, hemoglobin, indican, acetone, diacetic acid, and such microscopic elements as casts, pus, and red blood cells.

Amount.—The amount of urine excreted by normal adults varies from 1,200 to 1,500 c.c. per day. An increase in amount is known as *polyuria*, a decrease as *oliguria* and a complete suppression is known as *anuria*. Polyuria is most often seen in diabetes and chronic nephritis. Oliguria is most often seen in acute nephritis, fevers, and severe diarrheas.



Fig. 195.—Technician examining urine. The procedure being carried out is the determination of specific gravity. By means of the apparatus on the table in front of the technician, six albumin and six sugar tests may be made at one time.

Color.—As a rule, urine is of an amber color and the more highly concentrated it is, the deeper its color. Bloody urines are often brown, black, or smoky in color. In carbolic acid and lysol poisoning, the urine is of a brownish black color. The taking of methylene blue gives the urine a green color. In certain cases of melanoma the urine turns black on standing.

Appearance.—Normal urine is clear when passed. Upon standing a faint cloud forms and settles to the bottom. This is known as a “nubecula” and consists of epithelial cells,

mucus, and leucocytes. A turbidity when passed is due to the precipitation of phosphates or urates, or the presence of blood, pus, or bacteria.

Specific Gravity.—The normal specific gravity ranges from 1.013 to 1.023. Usually, the smaller the amount of urine passed, the higher the specific gravity, and the more urine passed, the lower it is. Diabetes mellitus is an exception to this rule because a large amount of urine of high specific gravity is passed. The high specific gravity is due to the large amount of sugar (glucose) in the urine.

Reaction.—Normal urine is acid in reaction and becomes alkaline on standing. Urine that is alkaline when passed may be due to the ingestion of certain foods and drugs or to the decomposition of urea by bacterial action. The latter would indicate an infection in some part of the urinary tract.

B. Normal Composition

The most important components of normal urine are water, urea, ammonia, uric acid, creatinine, chlorides, and phosphates. The amount of these substances in the urine may be decreased by (1) a decrease in the amount in the blood, or (2) diseases of the kidneys which reduce their excretory capacity. They may be increased by (1) an increase in the amount in the blood or, in rare instances, by (2) an increased permeability of the kidneys.

Formerly textbooks gave elaborate methods for the quantitative estimation of the normal components of the urine, but in recent years this has been replaced by their estimation in the blood. For this there are three reasons: (1) there is a definite relation existing between the amount of these substances in the blood and urine; for example, when the kidneys fail to excrete urea, uric acid, or creatinine, their amount in the blood increases; (2) the chemical methods used for their estimation in the blood are more reliable; and (3) the collection of a twenty-four-hour specimen of urine is avoided.

C. Abnormal Constituents of Urine

Certain abnormal constituents of the urine may be normally present in the blood without being excreted in the urine and appear in the urine not as a result of kidney dis-

ease but because the amount in the blood has increased to such a degree that the kidneys allow them to pass into the urine. A good example of this type of substance is glucose. Other substances appear in the urine as a result of disease of the kidney. Albumin is the best-known substance of this type.

Albumin.—When albumin is found in the urine, nephritis is always first thought of on account of the relation existing between albuminuria (albumin in the urine) and nephritis. Nothing, however, is more erroneous because albuminuria may be found in many other conditions. Albuminurias are divided into (1) true albuminurias, in which the renal cells are so altered that they liberate albumin themselves or allow it to escape from the blood plasma, and (2) false albuminurias, in which albumin containing materials gain access to the urine in some portion of the urinary tract. Such materials are blood, pus, bile, etc. True albuminurias may be due to primary disease of the kidneys or the effects upon them of disease in other parts of the body. Such effects are often brought about by fevers and certain poisons. So-called physiological albuminurias may follow prolonged exercise, cold baths, etc.

Sugar.—The student should remember that the term "sugar" does not indicate a particular compound but that it is a term applied to a group of related compounds which show considerable variation in characteristics. When we speak of "sugar in the urine" we usually refer to glucose (dextrose) which is the one by far the most frequently found and the one which appears in the urine of those having diabetes mellitus. It should be remembered that normal urine contains a small amount of glucose, but it is too small to be detected by the tests used in ordinary work. Lactose (milk sugar) may sometimes occur in the urine of nursing mothers.

Indican.—While often considered a normal constituent of the urine, normal urine does not give positive results with the ordinarily used tests for indican. Its presence indicates some type of protein decomposition, and it is most often found when intestinal putrefaction is present or absorption from the intestines is poor.

Acetone, Diacetic Acid, and Beta-oxybutyric Acid.—These compounds (collectively spoken of as the *acetone bodies*) are often found in association because they have the same origin. They represent products that are derived from the faulty catabolism of fats, and under normal conditions are completely destroyed. This incomplete catabolism is most often associated with faulty carbohydrate metabolism because carbohydrate metabolism is the source of the oxygen that oxidizes fats. The acetone bodies are of special importance on account of their association with diabetic and postoperative acidosis. Postoperative acidosis is much more likely to occur if acetone bodies are in the urine before operation. A marked increase of acetone bodies in the urine of a diabetic may be a sign of impending coma, and their narcotic action explains at least a part of the symptoms. Acetone bodies also occur in pernicious vomiting of pregnancy, starvation, and in the diarrheas of children.

Hemoglobin.—Hemoglobin may appear in the urine with or without red blood cells. *Hemoglobinuria* means the presence of hemoglobin in the urine and *hematuria* means the presence of red blood cells. Hemoglobinuria is most often associated with conditions producing marked blood destruction, such as malaria, certain poisons, the bites of certain snakes, and the transfusion of incompatible blood. *Malarial hemoglobinuria* is often spoken of as "black water fever." *Paroxysmal hemoglobinuria* is a condition in which the patient has paroxysms of hemoglobinuria without known cause. The paroxysms often follow exposure to cold. The condition is most frequent in those who have syphilis.

Bile.—Bile appears in the urine in many cases of jaundice. Jaundice and its causes are discussed on page 679.

Casts.—Casts never appear in a strictly normal urine, but their presence does not necessarily indicate a permanently diseased kidney. The casts most often seen are of the hyaline and granular types. Hyaline casts are the least significant of all. Granular casts indicate a degeneration of the epithelium of the tubules. If the disturbance is severe enough, epithelial cells may be attached to the casts (epithelial casts). Pus casts have attached pus cells and indicate a suppurative

condition within the kidney. Blood casts have attached red blood cells and indicate a hemorrhage into the kidney substance.

Pus.—Pus in the urine (pyuria) occurs most often in cystitis, pyelitis, urethritis, and tuberculosis of the kidney.

Red Blood Cells.—Red blood cells occur in the urine most often in nephritis, tumors of the urinary tract, tuberculosis, kidney stones, and bladder stones. Menstrual blood must be excluded before saying that a true hematuria exists.

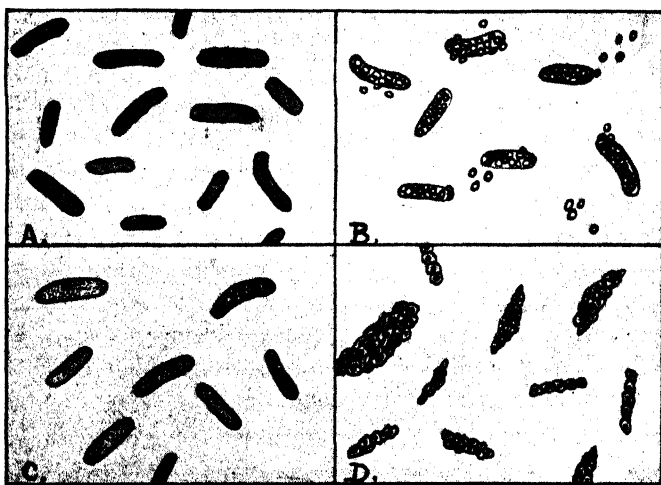


Fig. 196.—Urinary casts: A, Hyaline casts; B, pus casts; C, granular casts; D, epithelial casts.

Bacteria.—The important pathogenic bacteria which may be found in the urine are typhoid bacilli, tubercle bacilli, colon bacilli, staphylococci, and streptococci. Thirty per cent of those with typhoid fever excrete the bacilli in their urine, and in some cases the bacilli are excreted for years.

D. The Urine in Diabetes and Nephritis

1. **Diabetes.**—There are three conditions whose names contain the term “diabetes”: namely, diabetes mellitus,* dia-

*Diabetes mellitus is a disease of metabolism brought about by a failure of the pancreas to produce enough of its internal secretion, insulin, which controls sugar metabolism.

betes insipidus, and renal diabetes. The term "diabetes" as commonly used refers to diabetes mellitus.

Two erroneous ideas concerning glycosuria (glucose in the urine) and diabetes are prevalent: (1) the presence of glucose in the urine means that the patient has diabetes mellitus, and (2) diabetes mellitus is a disease of the kidneys. While a persistent glycosuria is most often due to diabetes mellitus, such is not necessarily the case, and transient glycosurias are frequently due to other causes.

Normally the blood contains from 90 to 120 mg. of glucose per 100 c.c., and a small amount, but not enough to be detected by the tests ordinarily used, passes into the urine. When the amount in the blood reaches a certain point, "the threshold point," the kidneys are unable to hold the glucose back any longer, and enough to be detected by ordinary tests spills over into the urine. The threshold point in normal persons lies between 160 and 180 mg. per 100 c.c. of blood. When the kidney function is impaired, the threshold point is higher. Therefore, with the exception of one condition (renal diabetes) the appearance of glucose in the urine indicates that the amount in the blood exceeds the threshold point. This increase may be due to increased intake (alimentary glycosuria) or impaired utilization, as occurs in diabetes mellitus.

In *diabetes mellitus* the high sugar content of the blood is associated with the excretion of large quantities of pale urine which contains sugar and is of a high specific gravity. Acetone is usually present in moderately severe cases, and diacetic acid and oxybutyric acid are present in very severe cases. It should be remembered that just as the diseased kidney loses its ability to excrete the waste products of the body, it also loses its ability to excrete sugar. It is for this reason that the quantitative estimation of the amount of glucose in the blood is of more value than the estimation of the amount in the urine.

In *renal diabetes* the amount of sugar in the blood is not above normal, but sugar is found in the urine. The cause of the condition is not known. Some workers think that it is a type of nephritis.

In *diabetes insipidus* large quantities of pale urine of a low specific gravity are excreted. It contains neither sugar nor albumin. Its exact cause is not known.

2. Nephritis.—The presence of albumin and casts is the most constant finding in all types of nephritis. The amount of albumin may vary from the slightest trace to an amount so large as to form a solid coagulum when the urine is boiled. The presence of casts is somewhat more significant of kidney damage than the presence of albumin. This is especially true if the casts are of the coarsely granular, blood, epithelial, or fatty varieties. It should be remembered that the presence of albumin may be due to many conditions other than nephritis and that a few hyaline or finely granular casts may mean nothing more than some slight circulatory disturbance of the kidneys. Even though this statement be true, the continued presence of albumin and casts should lead to a strong suspicion that nephritis exists. Hematuria is of common occurrence in nephritis.

Questions for Review

1. How do irritants causing nephritis reach the kidneys?
2. What are casts? What does their appearance in the urine signify?
3. What are the results of obstruction to one or both ureters?
4. What abnormal constituents usually appear in the urine in diabetes? In nephritis?
5. Enumerate symptoms of a pure nephrosis.

True-False Test

Place the word "true" or "false" before each statement.

- 1. Nephritis is a diffuse bilateral nonsuppurative inflammation of the kidneys.
- 2. Acute glomerulonephritis attacks primarily the glomeruli of the kidneys.
- 3. When the kidneys fail to excrete the nitrogenous wastes, they accumulate in the blood.
- 4. In the polyuria of nephritis the total amount of urine excreted is increased and, therefore, more wastes are excreted than normal.
- 5. Sugar is normally found in both urine and blood.
- 6. The normal blood sugar is about 80 to 120 mg. per 100 c.c. of blood.

- 7. When the blood contains around 160 mg. of sugar per 100 c.c., sugar begins to be excreted by the kidneys.
- 8. All substances which are normally found in the blood may normally appear in the urine.
- 9. The point at which sugar passes from the blood to the urine is spoken of as the threshold point.
- 10. The urine of a person suffering from diabetes insipidus contains both sugar and albumin.
- 11. Hyaline casts in the urine indicate a greater degree of destruction of the tubule of the kidneys than does either granular or epithelial casts.
- 12. A few casts may appear in normal urine.
- 13. The origin of the indican which appears in the urine is protein decomposition.
- 14. Acetone bodies are products of faulty metabolism of fats.
- 15. A definite relation exists between the amount of certain constituents of the urine and the amount of these substances found in the blood.
- 16. The amount of urine excreted in twenty-four hours varies greatly, but 3,000 c.c. is about the average daily output.
- 17. Anuria is a diminished amount of urine.
- 18. Oliguria is complete suppression of urine.
- 19. Normal urine has a specific gravity of 1.013 to 1.023.
- 20. In pyonephrosis the pelvis of the kidney is filled with pus.
- 21. Obstruction to the outflow of urine from the bladder is a predisposing cause of cystitis.
- 22. Hydronephrosis is dilatation of the pelvis of the kidney due to obstruction to the outflow of urine somewhere in the urinary tract.

References

- Boyd, William: A Textbook of Pathology, Philadelphia, 1947, Lea & Febiger.
- Anderson, W. A. D.: Synopsis of Pathology, St. Louis, 1946, The C. V. Mosby Co.
- Dodson, Austin I.: Synopsis of Genitourinary Diseases, St. Louis, 1945, The C. V. Mosby Co.
- Heitzmann, Louis J.: Urinary Analysis and Diagnosis, Baltimore, 1934, William Wood & Co.
- Gradwohl, R. B. H.: Clinical Laboratory Methods and Diagnosis, St. Louis, 1948, The C. V. Mosby Co.
- Barnes, Roger W., and Waichi, K. A.: Factors Influencing the Formation of Sulfonamide Urinary Concretions, J. Urol. 49: 324-333, 1943.

CHAPTER LVI

DISEASES OF THE FEMALE ORGANS OF REPRODUCTION

I. THE OVARIES

A. Inflammation

Ovarian Abscess.—Ovarian abscess is brought about by infection of a ruptured graafian follicle and is most often due to the extension of a gonorrheal salpingitis but may be due to puerperal sepsis. Adhesions may form about the ovary and tube in such a manner that an ovarian abscess and purulent salpingitis are converted into a single cavity. This is known as a *tubo-ovarian abscess*.

B. Cysts of the Ovary

Follicular Cysts.—When a graafian follicle develops but fails to rupture, its contents often liquefy and more fluid is poured into the follicle, which distends it and forms a cyst. These cysts may be single or multiple and are the most common cysts of the ovary. They are seldom more than 3 cm. in diameter, but occasionally a cyst may become so large as to stretch the entire ovary over its surface. Follicular cysts are filled with a clear, colorless fluid.

Corpus Luteum Cysts.—If cyst formation occurs after the ovum has been expelled and the processes leading to the formation of a corpus luteum have begun, a corpus luteum cyst results. These cysts are usually single, and their walls have a thick yellow lining. They are seldom very large, but hemorrhage into the cavity of the cyst may cause an ovarian hematoma.

C. Cystadenomas

About 80 per cent of the tumors of the ovary are glandular tumors in which so much fluid is secreted by the glandular epithelium that the glands become dilated into cysts. Such tumors are known as cystadenomas. Cystadenomas of the

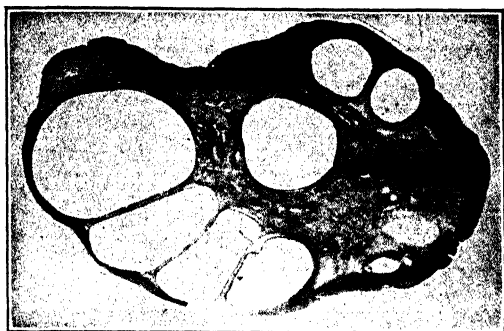


Fig. 197.—Follicular cysts of ovary. (From Crossen and Crossen: *Diseases of Women*. The C. V. Mosby Co.)

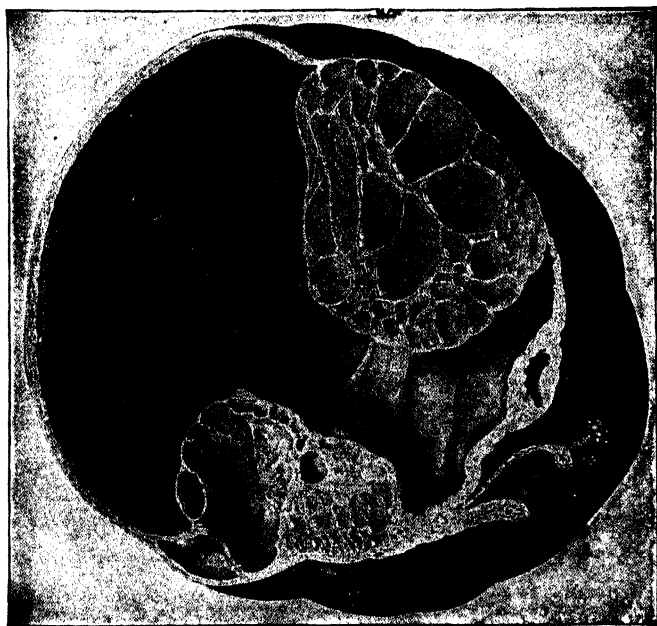


Fig. 198.—A pseudomucinous cystadenoma of the ovary. Note the development of secondary cysts in the wall of the large cyst. (From Crossen and Crossen: *Diseases of Women*, The C. V. Mosby Co.)

ovary are of two types: multilocular or pseudomucinous and papillary or serous, the terms multilocular and papillary referring to their structure while the terms pseudomucinous and serous refer to the contents of the cyst.

Multilocular (Pseudomucinous) Cystadenomas.—Multilocular cystadenomas are round or oval, lobulated tumors containing many cystic spaces filled with a thick, yellow, stringy mucoid material known as pseudomucin. These tumors are usually unilateral and pedunculated, and unless

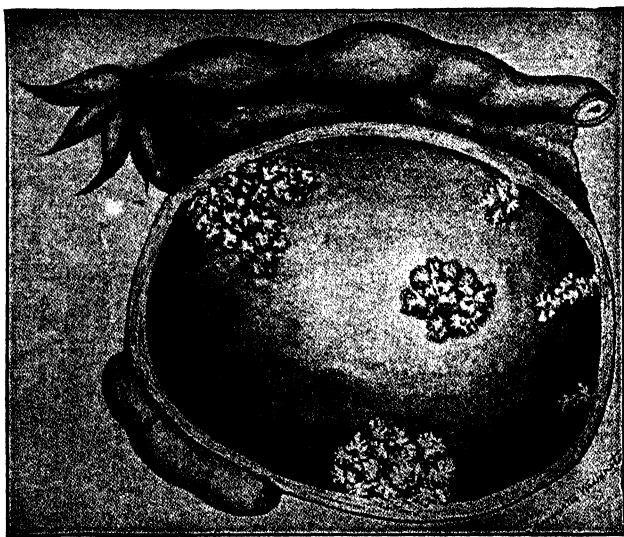


Fig. 199.—A papillary cystadenoma sectioned. Note the papillary structures growing from the lining of the large cyst. (From Crossen and Crossen: *Diseases of Women*.)

surgically removed may reach almost unbelievable size. They are not malignant in the ordinary sense, but spilling of their contents into the abdominal cavity gives rise to the condition known as pseudomyxoma peritonei which was discussed on page 688, and the tumor itself has a remarkable tendency to form adhesions with surrounding structures. This is by far the most common tumor of the ovary.

Papillary (Serous) Cystadenomas.—These tumors usually consist of a unilocular, thick-walled cyst with papillary pro-

jections extending from the lining into the cyst cavity, which is filled with a serous fluid. In some cases the papillary growths perforate the wall of the cyst and appear on its outside, from whence they spread to the peritoneum and cause widespread secondary growths and a rapidly developing ascites. Papillary cystadenomas are often bilateral and are seldom of greater size than a large orange. Due to the fact that they have a marked tendency to spread to the peritoneum and that more than 50 per cent recur after removal, papillary cystadenomas should be considered malignant tumors.

D. Carcinoma

Primary carcinoma of the ovary is not common. It occurs as a soft jellylike tumor that involves one ovary, then the other, and metastasizes to the uterus, peritoneum, and lumbar lymph nodes, producing early ascites and a rapidly fatal termination. On account of the frequency of metastasis to the uterus, a hysterectomy should accompany the removal of an ovarian carcinoma.

Secondary carcinoma of the ovary is much more common than primary carcinoma and is usually bilateral. It is most often secondary to carcinoma of the intestine or uterus.

E. Dermoid Cysts

Dermoid cysts may occur in fetal life or childhood but do not reach full development until after puberty. They form 10 per cent of all ovarian tumors and in some cases are bilateral. They consist of a rather thick-walled cyst that is filled with a yellow, puttylike material, often containing hair. Other structures found in dermoid cysts are sebaceous glands, rudimentary teeth, cartilage, bone, thyroid tissue, poorly developed eyes, etc. These structures will be found growing within or arising from a nipple-shaped mass, known as the *dermoid process*, which protrudes from the lining of the cyst and is covered with skin. The puttylike material in the cyst is secreted by the sebaceous glands. These tumors belong to the group of tumors known as teratomas. They rarely exceed the size of an orange and seldom cause symptoms.



Fig. 200.—Dermoid cyst of ovary. Notice bone, hair, and teeth.

II. THE FALLOPIAN TUBES

A. Salpingitis

Salpingitis or inflammation of the fallopian tubes is most often due to organisms that reach the lumen of the tubes by way of the uterine cavity, but some cases are due to organisms from the peritoneal cavity that reach the lumen by passing through the fimbriated extremities of the tubes. Like other inflammations, salpingitis may be acute or chronic.

Acute Salpingitis.—Fully 70 per cent of cases of acute salpingitis are due to gonococci which reach the tubes by way of the uterine cavity. Nongonorrheal salpingitis is usually due to streptococci, staphylococci, or *Bact. coli*. Streptococcus salpingitis usually follows a streptococcus infection of the puerperal uterus or an attempt to produce an abortion.

When a fallopian tube becomes infected, its walls undergo thickening and its fimbria becomes adherent, which closes the peritoneal extremity of the tube. By the time the peritoneal end of the tube is closed, swelling of the mucosa has

sealed the uterine end, and the lumen of the tube is converted into a closed cavity. If the inflammation is of a catarrhal nature, the cavity becomes filled with mucus, producing a *hydrosalpinx*. If it is of a purulent nature, the cavity becomes filled with pus, producing a *pyosalpinx* or "pus tube." Organisms often spread to the ovary and infect a ruptured graafian follicle, producing an ovarian abscess or a tubo-ovarian abscess if the peritoneal end of the tube has been closed by the adherence of the fimbria to the ovary. In gonorrheal salpingitis the pus becomes sterile within a few weeks after the onset of the disease.

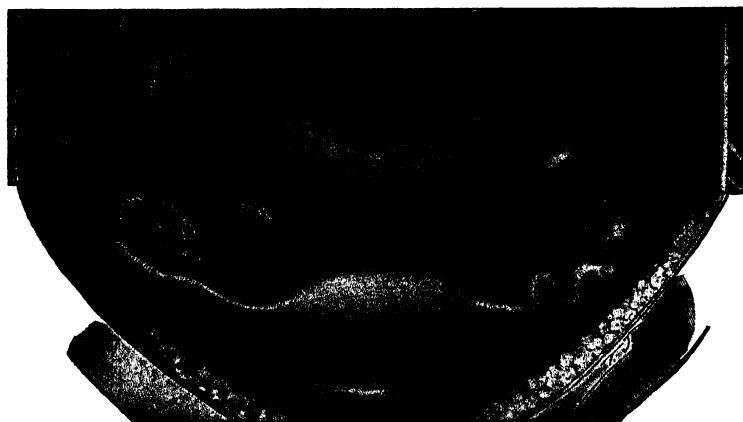


Fig. 201.—Acute salpingitis, of left fallopian tube. Compare with normal right tube. (From Crossen and Crossen: *Diseases of Women*.)

As a rule, both tubes are involved in acute salpingitis, and the infectious material may escape from the extremities of the tubes or pass through their walls to produce a local or general peritonitis. Adhesions of the rugae within the tubes often lead to the formation of crypts which may arrest the passing ovum. In some cases these adhesions may be so extensive as to cause complete occlusion of the tube.

Chronic Salpingitis.—Chronic salpingitis is usually a continuation of the acute form. It is characterized by marked thickening of the walls of the tubes, with the formation of extensive adhesions of the rugae and of the fimbria of the tubes and between the tubes and surrounding structures. In

such tubes purulent material may remain for a long time, producing a chronic pyosalpinx. Chronic salpingitis is of importance on account of its tendency to cause adhesions, sterility, and tubal pregnancy.

B. Tuberculous Salpingitis

Tuberculosis attacks the fallopian tubes more often than any other female generative organ. It is always secondary to tuberculosis in some other part of the body, most often the lungs, and is often complicated by tuberculous endometritis.

C. Ectopic Pregnancy

Normally the ovum is fertilized in the fallopian tube and passes to the uterus where the fetus develops. Rather frequently (about one time in three hundred pregnancies) the progress of the ovum is arrested in the tube, which causes a tubal pregnancy. Less often the ovum is fertilized outside of the fallopian tube and instead of entering the tube becomes attached to some abdominal structure where a placenta is formed and the fetus develops. This is known as a *primary abdominal pregnancy*. Pregnancies occurring outside the uterus are known as *ectopic* or *extrauterine* pregnancies. Of these, tubal pregnancies are by far the most common.

Chronic salpingitis is a common cause of tubal pregnancy because in this condition the folds within the tubes become thickened and matted together, forming pockets and recesses which entrap the ovum as it passes along the lumen. According to some investigators, tubal pregnancy is most often due to the presence of endometrial tissue in the mucosa of the fallopian tube. It is a well known fact that endometrium has a marked tendency to grow in places other than its normal location. When the fertilized ovum becomes arrested in the tube, development begins, chorionic villi burrow into the tubal wall, and the uterus shows a distinct decidual reaction and enlarges to the size of a two months' pregnancy.

On account of the anatomy of the tubes it is practically impossible for a tubal pregnancy to go to full term, and it ends most often by tubal abortion, but it may end by tubal

rupture. In *tubal abortion* the erosion of the wall of the tube brought about by the growth of the chorionic villi leads to hemorrhage into the gestation sac which converts it into a *tubal mole*. At the same time the tube becomes filled with blood. If the fimbriated extremity of the tube is open, the contractions of the tube expel the mole into the abdominal cavity. Rupture occurs in about 25 per cent of tubal pregnancies and is due to the destruction of a portion of the tubal wall by the erosive action of the chorionic villi. Rupture may be accompanied by enough hemorrhage and shock to cause the death of the patient. As a rule, the fetus is destroyed when the tube ruptures, but in rare instances the fetus is slowly extruded and remains alive, in which case the placenta may become attached to the abdominal viscera producing a *secondary abdominal pregnancy*.



Fig. 202.—Bilateral tubal pregnancy. Drawing showing the condition found at operation. Pregnancy near the middle of one tube and at the outer end of the other, both ruptured. Tubal abortion on left side. (From Crossen and Crossen: *Diseases of Women*.)

In abdominal pregnancy the placenta is so poorly developed that the fetus seldom reaches maturity but dries up and becomes infiltrated with lime salts, forming a *lithopedion*.

III. THE UTERUS

A. Hemorrhage

Increased menstrual hemorrhage is known as *menorrhagia* and is an accompaniment of certain general diseases, such as anemias, tumors, etc. Uterine bleeding not related to menstruation is known as *metrorrhagia* and may be caused by traumatism, local infections, and certain general diseases, but it is more often caused by cancer or fibromyomas of the

uterus. Any person with metrorrhagia without obvious cause should undergo a most thorough examination for cancer of the uterus, and this is especially true if the bleeding begins after the menopause.

Girls sometimes menstruate long before the age of puberty. This is known as *precocious* menstruation. In other cases the menstrual cycle is accompanied by hemorrhage from the nose, breasts, lungs, etc. This is known as *vicarious* menstruation.

The hemorrhage which occurs after detachment of the placenta ceases when the uterus contracts; it may continue indefinitely if the uterus does not contract properly or if a portion of the placenta fails to be expelled.

B. Endometritis and Endocervicitis

The lining of the uterine cavity (endometrium) and cervix (endocervix) differ in their structure, function, and reaction to disease but for the sake of brevity inflammation of both will be discussed under the heading of endometritis.

Acute Endometritis and Endocervicitis.—Acute inflammation of the endometrium occurs most often following childbirth or attempts at abortion but may occur unassociated with pregnancy. Acute endometritis following childbirth or attempts at abortion is most often due to streptococci of the hemolytic type.

Acute endometritis unrelated to pregnancy may be due to gonococci, necrosis of uterine tumors or polyps, or organisms introduced by unclean instruments. In gonorrheal infections the endocervix is chiefly involved and the inflammation begins as a catarrhal process which progresses to suppuration with the production of a large amount of greenish yellow pus. Acute gonorrheal endocervicitis often becomes chronic.

Chronic Endometritis and Endocervicitis.—Chronic endometritis is not as common as it was once thought to be because microscopic changes in the endometrium which were formerly thought to be due to chronic inflammation are now known to be normal premenstrual changes.

Chronic endometritis may be a continuation of the acute form or may arise without a previous acute attack. It may

be caused by gonococci, in which case the inflammation is practically always limited to the cervix, or it may be due to retained placental tissue, displacement of the uterus, or the degeneration of tumors or polyps.

Gonorrheal endocervicitis is very resistant to treatment and the cervix may remain infected long after the disease has been eradicated elsewhere. Such infections often come to light in the presence of the changes incident to pregnancy or the puerperium.

In addition to being the usual site of a chronic gonorrhea the exposed position of the cervix and the frequency with which it is lacerated during childbirth make it a frequent site of chronic nongonorrheal inflammation.

Frequently the openings of the glands of the inflamed endocervix become blocked, and their secretion distends them into cystlike structures. These are known as *nabothian cysts*.

C. Fibromyomas

Uterine fibromyomas, usually spoken of as "fibroids," are benign tumors made up of varying proportions of connective tissue and smooth muscle fibers. They may occur beneath the endometrium (submucous fibromyomas), in the uterine wall (interstitial or mural fibromyomas), or project from the outer surface of the uterus (subserous fibromyomas). In their beginning, submucous and subserous fibromyomas occupy an interstitial position.

Uterine fibromyomas are the most common of all tumors. They occur between the age of puberty and the menopause and are more common in women who have not had children. Fibromyomas seldom arise in the cervix.

Fibromyomas of the uterus are sharply separated from the surrounding tissue by a capsule. If they have not undergone degenerative changes, they are white and glistening in appearance. Those containing a large amount of connective tissue are extremely hard. They are benign in the pathological sense but may cause marked deformity of the uterus, give rise to pressure symptoms (constipation and malposition of the uterus), interfere with conception, produce abortion, obstruct labor, and cause extensive bleeding.

Submucous fibroids cause almost continuous bleeding from the endometrium, and in some cases may produce an increase in size of the uterus that is easily mistaken for pregnancy.

Subserous fibroids are usually multiple and may reach an enormous size. They may project from the uterus as knob-like processes or be attached to it by a distinct pedicle. They cause marked deformity and displacement of the uterus, but ordinarily do not interfere with menstruation and conception.

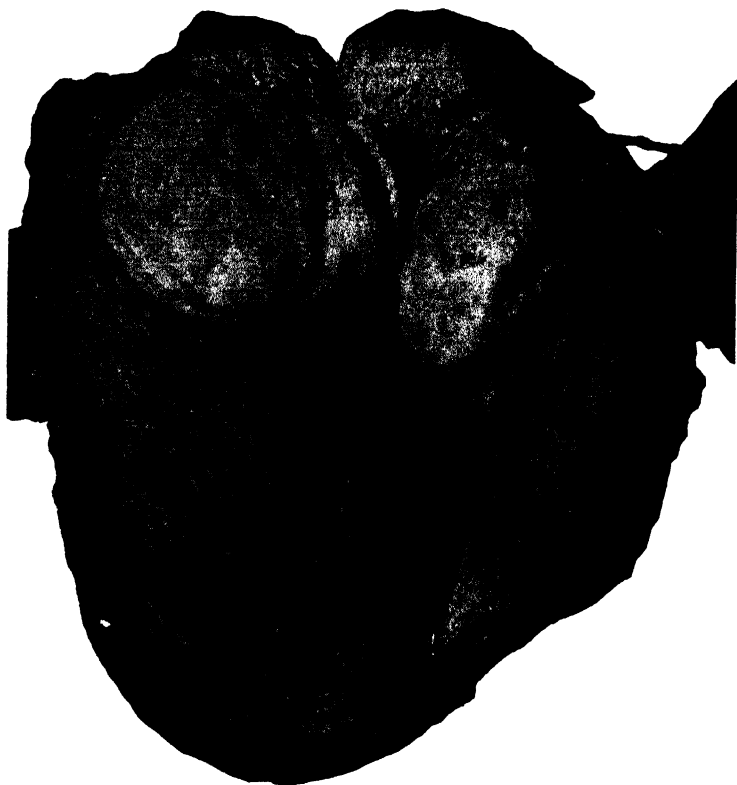


Fig. 203.—Opened uterus showing a large submucous fibromyoma. (From Crossen and Crossen: *Diseases of Women*.)

Fibroids may undergo atrophy or hyaline degeneration and portions may become liquefied, producing cysts. Calcification and sarcomatous degeneration sometimes occur. Fibromyomas sometimes undergo a rapid necrosis, the onset of which is an-

nounced by sudden pain and tenderness, and on section the fibroid has the appearance of a beefsteak. This is known as "*red degeneration*." Sometimes a fibroid will take on a rapid growth during pregnancy. After childbirth the fibroid may remain large or return to its former size.

D. Polyps

The term "polyp" is applied to a heterogenous group of growths and is based more on the shape of the growths than on their microscopic structure. Included under this term are pedunculated fibroids, fungoid and polypoid forms of endometritis, and papillomas of the endometrium.



Fig. 204.—Advanced cancer of cervix. Note ulceration. (From Crossen and Crossen: *Diseases of Women*.)

E. Carcinoma

Carcinoma (cancer) of the uterus occurs in two distinct forms: carcinoma of the cervix and carcinoma of the body of the uterus.

Carcinoma of the Cervix.—Fully 95 per cent of cases of carcinoma of the cervix arise in women who have had children, and in the majority of cases it begins at the site of a laceration caused by childbirth. It usually occurs between the forty-fifth and fiftieth years of life and with the exception of the breast is the most common site of cancer in women.



Fig. 205.—Cancer of body of uterus. The cancer is growing in the wall and projecting into the uterine cavity. (From Crossen and Crossen: *Diseases of Women*.)

Carcinoma of the cervix is usually of the squamous type and may occur as (1) an induration of the cervix, (2) an ulcerated area, or (3) a cauliflower-like growth protruding from the cervix. Cancer of the cervix grows more rapidly than cancer of the body of the uterus and growth is more rapid in the comparatively young than in those who are older. It often begins on the surface of the cervix and invades the

deeper tissues after which the cervix becomes converted into a funnel-shaped ulcer, the apex of which points toward the body of the uterus.

The first sign of cancer of the cervix is usually a watery, blood-tinged discharge. Unfortunately when this sign appears, ulceration has already occurred. As the disease progresses, bleeding increases, the discharge becomes fetid, and a severe cachexia develops. Extension to the bladder, rectum, vagina, and pelvic lymph nodes, draining the cervix, occurs early, and pyogenic infection of the cancerous mass is common. The presence of pain means that the cancer has spread beyond the confines of the cervix. Involvement of the body of the uterus is rare. Secondary growths in the lungs and liver may occur. Death ordinarily takes place within eighteen to twenty-four months after the cancer is recognized unless proper treatment is instituted.

Carcinoma of the Body of the Uterus.—This type of carcinoma forms about 10 per cent of the uterine cancers and is more common in women who have not had children. It occurs later in life than carcinoma of the cervix, often after the menopause, at which time any bleeding from the uterus is abnormal, and on account of this bleeding, is often recognized earlier than cancer of the cervix.

Cancer of the corpus uteri usually begins at the fundus and grows into the cavity of the uterus as a soft cauliflower-like mass that may fill the entire cavity. It then invades the wall of the uterus, which it may penetrate, and thus spread to the peritoneum. In structure, carcinoma of the body of the uterus is usually an adenocarcinoma; i.e., a carcinoma made up of glandular structures.

Cancer of the body of the uterus grows more slowly than cancer of the cervix and has much less tendency to ulcerate and invade the surrounding organs. This with its frequent earlier recognition makes cancer of the body of the uterus a much less formidable disease than cancer of the cervix. When metastasis does occur, it is to the pelvic lymph nodes and the ovaries. It seldom spreads to the cervix.

F. Chorionepithelioma

Chorionepithelioma is a peculiar tumor that arises from the covering cells of the chorionic villi and occurs at the placental site. It usually occurs after the expulsion of a hydatidiform mole but may occur after an abortion or normal delivery or even during pregnancy. In some cases it occurs immediately after the expulsion of a mole, an abortion, or a normal delivery, but in most cases its occurrence is delayed for three or four months. It usually occurs in multiparas past forty.

Chorionepithelioma occurs as a soft mass somewhat resembling placental tissue that infiltrates the uterine wall and projects into the uterine cavity.

In some cases growth is rapid and metastasis to the external genitalia and lungs occurs early, while in other cases the tumor is comparatively benign. Complete hysterectomy sometimes stops the spread of apparently highly malignant chorionepitheliomas. Both primary tumor and metastasis have been known to disappear spontaneously. Abnormal bleeding or severe hemorrhage often leads to a diagnosis.

IV. THE VAGINA

Vaginitis

Acute Catarrhal Vaginitis.—Acute catarrhal vaginitis may be due to gonococcus infections, mechanical or chemical irritation, or highly irritating uterine discharges. Primary gonococcus vaginitis is common in children but the gonococcus vaginitis of adults is usually secondary to gonococcus urethritis or cervicitis, and even when both of these are present the vagina may show little involvement.

Pseudomembranous Vaginitis.—As a result of certain infectious diseases, pressure necrosis, and infections occurring during labor the vaginal mucosa may become more or less extensively covered with a dirty pseudomembrane. This is known as pseudomembranous vaginitis. Vaginal infections due to *C. diphtheriae* are of this type.

Chronic Vaginitis.—Chronic vaginitis may follow acute attacks of the disease or may be due to neglected pessaries,

irritation by uterine discharges, or the use of too strong douches. Long-standing cases often lead to vaginal erosion and cicatricial contraction ending in stenosis.

Trichomonas Vaginitis.—In certain intractable cases of vaginitis with a cream-colored, foamy discharge, *Trichomonas vaginalis* is found in abundance. Some observers believe that this organism is the specific excitant of this type of vaginitis, while others consider it a harmless secondary invader. My own view is that it may appear in either rôle, more often in the former.

Monilia Vaginitis.—Vaginitis due to monilia is of considerable frequency in diabetes and pregnancy.

V. THE MAMMARY GLANDS

A. Acute Mastitis

Acute inflammation of the breast may occur in the form of a diffuse process or as an abscess. Diffuse inflammation is usually due to streptococci while abscesses are usually due to staphylococci. Fully 90 per cent of cases of acute mastitis occur during the first few weeks of lactation, and the causative bacteria gain access to the breast by fissures in the nipple.

When abscess formation occurs only one abscess may be present, or there may be several that are discrete or that communicate with each other. Mammary abscesses usually discharge on the surface, but in some cases they open into the pleural cavity. If an abscess communicates with a lactiferous duct, there may be a purulent discharge from the nipple.

Occurring less often than the types of mastitis previously discussed are mastitis of the newborn and the hematogenous mastitis occurring as a complication of typhoid fever, scarlet fever, and mumps. The habit of expressing the secretion of the breast of the newborn, at one time practiced by midwives, often leads to an acute purulent mastitis.

B. Chronic Mastitis

Chronic mastitis is one of the many names given to a closely related group of conditions, some of which represent perversions of involution while others, but fewer, are probably of inflammatory origin.

Chronic mastitis most often begins near the menopause, and the patient may complain of a lump in the breast or pain which is slightly worse at menstruation. More than one lump may be present and both breasts may be involved. The breast has a granular, indurated feel, and when it is incised a great increase in connective tissue with cysts of varying size is found. The larger cysts may have papillomatous processes growing from their wall.

The relation of chronic mastitis to cancer of the breast is a disputed question. Some authorities insist that chronic mastitis is so frequently a forerunner of cancer of the breast that it should be considered a precancerous condition, while others hold that cancer is of no greater frequency in breasts affected with chronic mastitis than in those that are not.

C. Discharges From the Nipple

Almost half of the bloody discharges from the nipple are due to cancer. The remainder are due to traumatism, benign tumors, and disturbances of the breast at the menstrual period. Bleeding from the nipple at the menstrual period is usually attributed to vicarious menstruation, but many of these cases are probably due to the hyperemia of the breast which occurs at that time. A chocolate discharge may occur in chronic mastitis, and a purulent discharge may occur when an abscess breaks into a milk duct.

D. Fibroadenoma

Fibroadenoma is the most common benign tumor of the breast. It occurs as a freely movable, circumscribed, well-encapsulated mass of glandular and connective tissue, which grows slowly and gives rise to few symptoms, often being accidentally discovered. Fibroadenomas seldom exceed a size greater than 3 cm. in diameter.

There are two types of fibroadenomas: the pericanalicular, in which the increase in connective tissue is most pronounced around the ducts, and the intracanalicular, in which connective tissue growths project into the ducts and elongate and distort them. Occasionally a fibroadenoma becomes cancerous.

E. Carcinoma

Carcinoma of the breast is one of the most common forms of malignant tumor and, when recognized late and improperly treated, one of the most fatal. It is most common in women within the age period of 40 to 49 years, but it is not uncommon in young women and is often seen in the aged. It occurs in three forms: (1) scirrhus, in which there is a superabundance of connective tissue that isolates the cancer cells in small groups, (2) encephaloid or medullary, in which there are broad strands of cancer cells with little intervening connective tissue, and (3) adenocarcinoma, in which there is a lawless multiplication of the glandular structures of the breast with invasion of the stroma. Two or even all of these forms may be found in a single breast. In addition to these forms of breast cancer, Paget's disease of the nipple is frequent enough to be of clinical importance.

There are a number of conditions which seem to predispose to carcinoma of the breast. Among these are previous disease of the breast, stagnation of secretion, endocrine disturbances, and abnormal lactation. Stagnation of secretion with consequent inflammation seems to act as an excitant of carcinoma. Recent evidence seems to indicate abnormal activity or overaction of the ovaries may bring about carcinoma of the breast.

Carcinoma of the breast enlarges by infiltrating the surrounding breast tissue, overlying skin and underlying muscles. Involvement of the skin leads to ulceration, and involvement of the underlying muscles leads to fixation to the chest wall. Later metastasis occurs by the lymphatics to the supraclavicular, axillary, and mediastinal lymph nodes. When the lymph nodes become involved, it is only a short time until secondary growths occur in far distant points, such as lungs, liver, and bones. Carcinomas of the medial portion of the breast are more dangerous than those in the outer part of the breast because they may metastasize directly to the mediastinal lymph nodes.

Scirrhus carcinoma, which is the most common form of breast cancer, begins as a hard freely movable nodule, usually in the upper, outer quadrant. It extends in an irregular manner and involves the underlying muscles and over-

lying skin. Involvement of the large milk ducts leads to retraction of the nipple and induration of the breast. Involvement of the supraclavicular and axillary lymph nodes occurs in late cases. The tumor grows rather slowly, and



Fig. 206.—Scirrhus carcinoma of breast. The main tumor is situated below a much indrawn nipple. There are several smaller outlying masses, the result of lymphatic spread. (From Boyd, William: *Surgical Pathology*. W. B. Saunders Co.)

the breast is small, hard, and flattened. On section the cancerous area cuts with resistance and is white, with extensions into the surrounding tissue. Microscopically scirrhus cancer of the breast is characterized by the presence of few can-

cer cells and a superabundance of connective tissue, which has the appearance of being engaged in an attempt to destroy the cancer cells.

Medullary, encephaloid or soft cancer of the breast grows rapidly, quickly invades the skin, ulcerates, and appears on the outside as a fungating mass. Lymph node involvement occurs early. Microscopically encephaloid carcinoma is characterized by the presence of wide strands of rapidly growing cancer cells and a small amount of connective tissue. This tumor quickly kills. An acute form of medullary carcinoma of the breast sometimes develops during lactation.

Adenocarcinomas of the breast may be solid or cystic. They grow rapidly and may become transformed into the medullary type.

Paget's Disease of the Nipple.—This condition begins as a red, unruly, eczematous condition of the nipple, which is usually followed by cancer of the breast, often at a distance from the nipple. Whether the cancerous condition is due to irritation produced by the eczema or the eczema is a result of the cancer is a disputed question.

F. Cysts

Cysts of the breast may be due to retention of secretions, inflammation, tumor growths, or abnormal involution. Encapsulation of abscesses or hemorrhages may lead to the formation of pseudocysts. Obstruction of a milk duct leads to the formation of a cyst filled with a liquid resembling milk. Such cysts are known as *galactoceles*.

Questions for Review

1. What is a dermoid cyst?
2. Explain the formation of a pyosalpinx.
3. What are two varieties of ovarian cysts? Are they malignant?
4. What is a common cause of ectopic pregnancy?
5. By what channels do bacteria reach the uterus and fallopian tubes?
6. What are "fibroids"? Name three varieties.
7. What are the early symptoms of carcinoma of the cervix?
8. What are three varieties of carcinoma of the breast?
9. What is a hydatidiform mole?

True-False Test

Place the word "true" or "false" before each statement.

- 1. The causative agent of salpingitis is always the gonococcus.
- 2. Fibroids are malignant tumors of the muscles and connective tissue of the uterus.
- 3. Fibroids occur more frequently in women of the colored race than in those of the white race.
- 4. Carcinoma of the cervix is more likely to occur in women from forty to fifty years of age, while carcinoma of the body of the uterus most often occurs in women from fifty to sixty years of age.
- 5. Carcinoma of the cervix is more common in women who have had children.
- 6. Salpingitis may be of tuberculous origin.
- 7. Chorionepithelioma is a very malignant tumor arising from the chorionic villi at the site of the placenta during pregnancy or soon after.
- 8. Endometritis is an inflammatory condition of the lining of the cervix.
- 9. Carcinoma of the breast is most likely to occur in the involuting breast.

References

- Boyd, William: Surgical Pathology, Philadelphia, 1947, W. B. Saunders Co.
- Foot, N. Chandler: Pathology in Surgery, Philadelphia, 1945, J. B. Lippincott Co.
- Crossen and Crossen: Diseases of Women, St. Louis, 1943, The C. V. Mosby Co.
- Cooke, Willard E.: Essentials of Gynecology, Philadelphia, 1943, J. B. Lippincott Company.
- Rose and Carless: Manual of Surgery, New York, 1943, William Wood & Co.
- Behan, R. J.: Cancer of the Breast, 1938, The C. V. Mosby Co.
- Ackerman and del Regato: Cancer, Diagnosis, Treatment, and Prognosis, St. Louis, 1947, The C. V. Mosby Co.
- Geschickter, Charles F.: Diseases of the Breast, Philadelphia, 1945, J. B. Lippincott Company.

CHAPTER LVII

DISEASES OF THE MALE ORGANS OF REPRODUCTION

I. THE TESTIS AND EPIDIDYMITIS

A. Inflammations

Inflammation of the body of the testis is known as *orchitis*. Inflammation of the epididymis is known as *epididymitis*. Inflammations of the testis may be classified as (1) those confined to the epididymis, of which gonorrhea is the best example, (2) those confined to the body of the testis, of which mumps and syphilitic orchitis are examples, and (3) those affecting both epididymis and body.

Acute Epididymitis.—Gonorrheal epididymitis is the most common type of acute epididymitis and is the most common complication of gonorrhea. It is usually secondary to a posterior urethritis and is usually unilateral but may be bilateral. Properly treated, acute gonorrheal epididymitis is usually cured without any permanent defect of the involved organ, but in some cases scarring may be so great as to obstruct the passage of spermatozoa. A bilateral epididymitis of this type leads to sterility. As a rule, the body of the testicle is not involved.

Acute Orchitis.—Acute orchitis occurs most often as a complication of mumps or typhoid fever. In many cases it leads to atrophy and fibrosis of the testis with loss of function. Bilateral orchitis with atrophy fibrosis and loss of function causes sterility. In certain other types of acute orchitis supuration with abscess formation may occur.

Chronic Orchitis.—Chronic orchitis may be a continuation of the acute form, but many cases arise without antecedent attacks and many cases are due to syphilis.

B. Tuberculosis

In the great majority of cases tuberculosis of the testis is secondary to tuberculosis in some other organ, especially the

lungs. It usually begins in one epididymis from which it spreads to the other epididymis and other parts of the genital system. As a rule, the body of the testis is not involved until the disease is far advanced.

Tuberculosis of the genital tract does not have the natural tendency to heal that tuberculosis has in many other parts of the body but remains ready to spring into activity on the slightest provocation.

C. Syphilis

Syphilis of the testis is rather common. It occurs as a diffuse inflammation or as single or multiple gummas, and the process is usually confined to the body of the testis. Diffuse inflammations are more frequent, but gummas are more often recognized because they cause testicular enlargement, while diffuse inflammations have little effect on the size and shape of the testis until far advanced, at which time testicular atrophy is brought about.

D. Tumors

Formerly, it was thought that all tumors of the testicle were sarcomas and highly malignant. It is now known that most of them are of the teratoid or mixed type because they usually arise from totipotential cells, i.e., cells capable of giving rise to all three embryonic layers. Testicular tumors may progress slowly or one or more elements may become malignant. Chorionepithelioma, a tumor ordinarily arising in the uterus, is a rare but most interesting testicular tumor. Dermoid cysts of the testicle have the same characteristics as in other parts of the body. Undescended or misplaced testes are more often the site of tumors than normal testes.

E. Hydrocele

During its descent to the scrotum the testis becomes invested with a peritoneal sac known as the tunica vaginalis. In most cases the sac becomes separated from the peritoneal cavity, but in some cases a communication between the two remains. This sac sometimes becomes filled with a large

amount of clear, yellow fluid, and the condition is spoken of as *hydrocele*. Acute hydrocele is most often due to a tuberculous or gonorrheal involvement of the testis. Chronic hydrocele may follow the acute form, but most cases come on without apparent cause. In some cases in which the opening between the peritoneal cavity and tunica vaginalis has not closed, the fluid is derived from the peritoneal cavity. In acute hydrocele the amount of fluid seldom exceeds 100 c.c., and it may be turbid or frankly purulent. In chronic hydrocele the fluid is clear and of a yellow color. The amount usually ranges from 100 to 300 c.c., but may reach liters. Hydrocele causes enlargement and deformity of the scrotum, and in long-standing cases, pressure causes atrophy of the testis.

Due to trauma, such as kicks, blows, or tapping, blood may escape into the hydrocele sac which converts the hydrocele into a hematocele.

F. Varicocele

Varicocele is a condition of varicosity of the veins of the spermatic cord. It is most common in young men and usually occurs on the left side. The veins become irregularly dilated and varicose, producing a large twisted tortuous mass. While there are many theories of the causation of varicocele, none is generally accepted. A few cases are due to pressure exerted on the spermatic vein by an abdominal tumor.

Varicocele is characterized clinically by reflex disturbances and a sensation of weight and pain. These symptoms may render a patient of a nervous temperament unfit to perform even moderate work.

II. THE PROSTATE GLAND

A. Inflammation

Acute Prostatitis.—Acute prostatitis is most often due to the extension of a gonorrheal posterior urethritis but may be due to other causes, such as infection of the posterior urethra by a catheter. Much less frequently it occurs as a hematogenous infection in septicemias and pyemias.

Acute prostatitis may occur as a simple inflammation or in a suppurative form. Small abscesses occurring in suppurative prostatitis may become encapsulated and larger ones may point in the perineum or rupture into the urethra. Swelling of the prostate leads to considerable pain and compresses the urethra, interfering with urination.

Chronic Prostatitis.—Chronic prostatitis is most often a continuation of the acute form and is a common accompaniment of prostatic hyperplasia.

Tuberculosis.—Tuberculosis of the prostate is a common disease and often extends from the prostate to other sexual organs.

B. Enlargement of the Prostate

Enlargement of the prostate usually occurs in men past their fiftieth year. There are many theories as to its cause, but when the subject is finally clarified it will probably be found that it may be brought about by several different causes. It is apparently no more common in those who have had gonorrhea than in those who have not.

In some cases the enlargement is due to an increase in the glandular structures of the prostate; in others it is due to an increase in the stroma, but in most cases there is an increase in both. The enlargement may be smooth or nodular, general or localized. The most important localized form is an enlargement of the middle lobe which projects under the posterior urethral wall as a rounded elevation or obstructing bar.

Prostatic hyperplasia, often incorrectly spoken of as prostatic hypertrophy, interferes with urination, and this is specially true when the middle lobe is enlarged. Obstruction to urination leads to hypertrophy and dilatation of the bladder, cystitis, and ascending infection. When the middle lobe projects upward a depression in the floor of the bladder is formed behind the enlarged lobe. This depression contains a small amount of urine known as *residual urine* which cannot be expelled during urination. Residual urine is prone to undergo decomposition and become infected, which leads to cystitis. Enlargement of the prostate leads to loss of renal

function and in more than 15 per cent of cases the prostate shows cancerous changes. Repeated catheterization, which is often necessary in prostatic enlargement, leads to cystitis.

C. Cancer

More than 15 per cent of enlarged prostates become cancerous. After the cancer becomes well established, it progresses rapidly with extension to the bladder, rectum, and seminal vesicles and metastasizes to the bones and regional lymph nodes. The results of the treatment of carcinoma of the prostate gland with stilbestrol and by castration indicate that the secretions of certain endocrine glands may be a factor in the production of the disease.

Questions for Review

1. What is epididymitis? Orchitis?
2. Give some of the causes and some of the results of acute epididymitis and acute orchitis.
3. Discuss tuberculosis of the testis. Syphilis.
4. What is a hydrocele? Give some of the causes.
5. What is a varicocele? Give some of the symptoms.
6. To what is prostatic enlargement due? Are enlarged prostates likely to become cancerous?
7. To what locations do cancer of the prostate spread?

Reference

Dodson, Austin I.: Synopsis of Genitourinary Diseases, St. Louis, 1945, The C. V. Mosby Co.

CHAPTER LVIII

THE ENDOCRINE GLANDS

I. INTRODUCTION

Instead of passing out of the gland by a duct, the secretory products of certain glands are absorbed directly into the blood. Such secretions are known as *internal secretions* and glands such as the thyroid, pituitary, and adrenals, which rid themselves of their secretions in this manner, are known as ductless glands. It has been found that certain glands which have ducts and produce external secretions also produce internal secretions. For this reason the term *endocrine glands*, which denotes glands producing internal secretions regardless of whether or not they produce external secretions, is gradually replacing the term ductless glands. Glands other than those already mentioned which have an endocrine function are the thymus, gonads, and pancreas.

There is a complicated interrelation existing between the endocrine glands, and the action of one is often profoundly influenced by the secretion of another. This interaction of the endocrine glands, as well as the functional activity of the individual glands, is at best imperfectly understood. The action of one gland may be increased or suppressed by changes within the gland itself or the influence of the secretions of other glands acting on it.

The internal secretions have been classified as *hormones*, i.e., substances which, having been formed in one part of the body, are carried in the blood to another organ or tissue whose activity they influence.

II. THE THYROID GLAND

A. Physiology

The thyroid gland is made up of closed vesicles which are normally filled with a colloid material that contains thyroxin. Thyroxin is an iodine-bearing compound upon which the functional activity of the gland depends. When an excessive

amount of thyroxin is absorbed into the blood, *hyperthyroidism* develops. When an insufficient amount is absorbed, *hypothyroidism* results.

The thyroid, at least in part, controls metabolism and body growth and exerts an influence over the nervous system and the development of the sex glands. It undergoes hypertrophy at puberty, also during menstruation and pregnancy. It undergoes atrophy in old age.

B. Goiter

The term *goiter* does not refer to a specific disease but merely indicates an increase in the size of the thyroid gland.

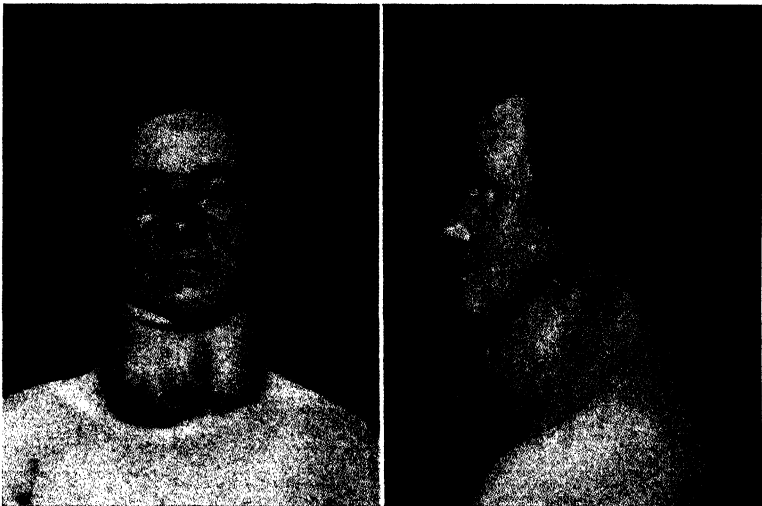


Fig. 207.—Patient with endemic goiter. (From Joll: Diseases of the Thyroid Gland, The C. V. Mosby Co.)

This increase in size may be due to an increase in colloid or an overgrowth of the tissue of the gland with a reduction in colloid. The former is known as *simple*, or *colloid*, goiter and the latter is known as *hyperplastic* goiter. Colloid goiters usually produce hypothyroidism, while hyperplastic goiters usually produce hyperthyroidism, which is most typically exemplified in exophthalmic goiter, or Graves' disease.

Colloid goiters are endemic in certain districts as Switzerland and the Great Lakes region of the United States where

the food and water are deficient in iodine. It is thought that when the food does not contain sufficient iodine the thyroid produces colloid but not thyroxin and attempts to compensate for the deficiency in thyroxin by producing an excess of colloid. These goiters may be prevented by adding sufficient iodine to the food supply. Iodine also has some curative action, but the goiter returns when iodine is discontinued. Endemic goiters usually appear in girls shortly before or at the time of puberty.

C. Hypothyroidism

A congenital deficiency in thyroid secretion leads to *congenital myxedema*, or *cretinism*, which is characterized by

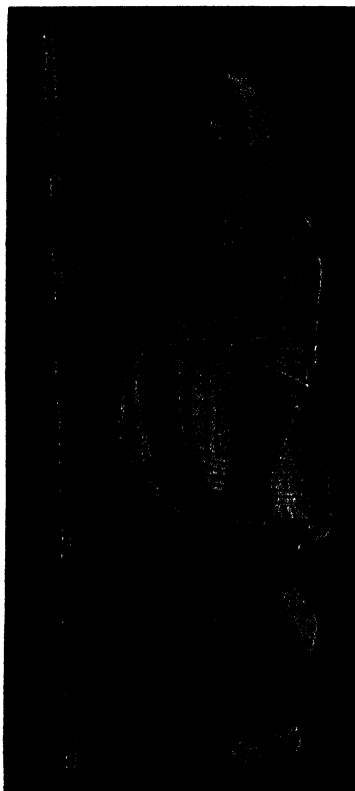


Fig. 208.—Cretin, 19 years of age. (From Bard: *MacLeod's Physiology in Modern Medicine*, The C. V. Mosby Co.)

slow development of bones, late closure of the fontanel and cranial sutures, dwarfism, delayed dentition, thickness of lips and tongue, thick pasty skin, lack of hair, low body temperature, extreme susceptibility to cold, low basal metabolism, and a retarded mentality. Symptoms make their appearance about the sixth month. Endemic cretinism is common in areas of endemic goiter. Cretins may have simple goiters or their thyroids may be absent or hypoplastic. The administration of thyroid extract prevents cretinism and transforms young cretins into normal children. Cretinism may be prevented also by feeding the mother iodine during pregnancy.

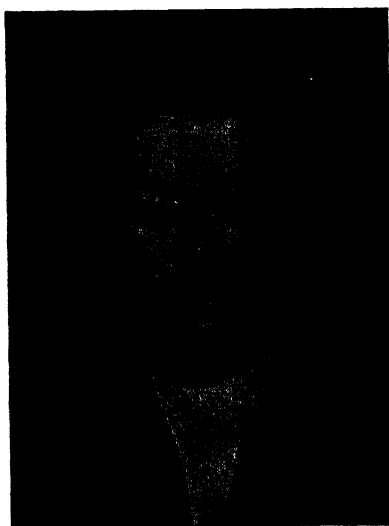


Fig. 209.—Patient with myxedema. (Courtesy Dr. L. M. Hurxthal, Lahey Clinic, Boston.)

When thyroid deficiency develops in later life, the skin becomes puffy and dry, the eyelids swell, the tongue and lips become thickened, the hair falls out, the sexual functions decline, nervous symptoms develop, the body temperature and basal metabolism fall below normal, and the patient becomes extremely susceptible to cold and slows down in thinking, perception, and motion. This is known as *myxedema* and may be due to a loss of thyroid function brought about by disease or surgical removal of the gland.

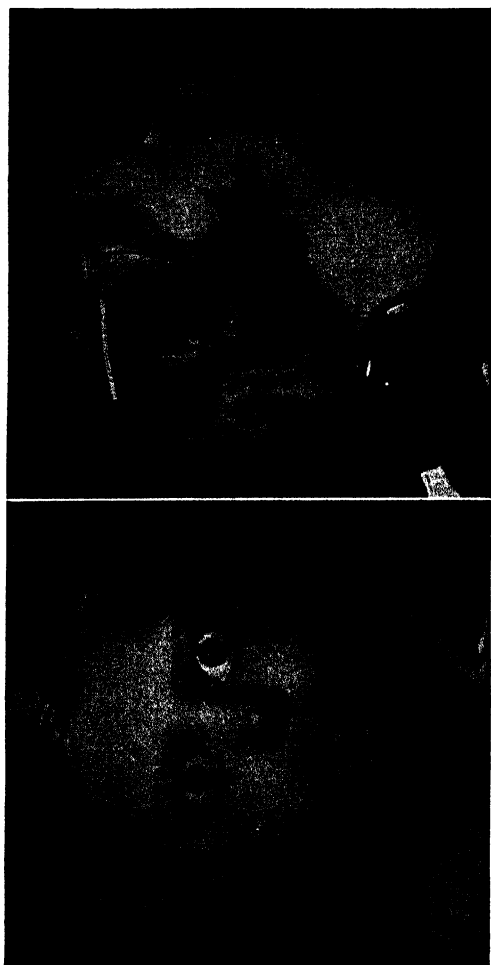


Fig. 210.—Patient with exophthalmic goiter. Notice prominent eyes and enlargement of neck.
(Courtesy Dr. L. M. Hurxthal, Lahey Clinic, Boston.)

Myxedema due to surgical removal of the gland is known as *cachexia strumipriva*. Myxedema shows marked improvement under thyroid medication, but, as is the case in cretinism, the hypothyroid state returns when medication is discontinued. The thyroid gland may be enlarged in myxedema but the enlargement is due to the accumulation of inert material.

Many otherwise normal persons have a slight degree of thyroid deficiency. Such persons often have a pasty appearance, do not think rapidly, move slowly, and complain of various nervous manifestations. They are extremely susceptible to cold, and their heart rate and basal metabolism are below normal.

D. Hyperthyroidism

Hyperthyroidism is due to an increased absorption of the active principle of the thyroid gland and leads to a hyperactivity of many parts of the body, especially the heart and nervous system. Hyperthyroidism is characterized by hypertrophy of the thyroid gland, tachycardia, profound nervous disturbances, increased basal metabolism, cardiac hypertrophy, loss of weight, weakness, and attacks of profuse sweating. A special form of the disease in which, in addition to the above symptoms, exophthalmos is present is known as *exophthalmic goiter*, or Graves' disease. The hyperactive gland eventually becomes exhausted and a state of hypothyroidism develops.

The cause or causes of the development of the hyperthyroid state are not known. Administration of iodine leads to a temporary reaccumulation of colloid and abatement of symptoms, but its injudicious use may lead to grave damage. Hyperthyroidism may be experimentally produced by the administration of thyroid extract or thyroxin.

E. Carcinoma

Carcinoma usually originates in a thyroid gland already the seat of a goiter. It grows rapidly and quickly leads to pain and fixation of the gland. Metastasis to the lungs and bones, especially the skull and vertebrae, occurs early.

III. THE PARATHYROID GLANDS

The parathyroid glands are four small organs that are usually loosely attached to the thyroid gland but may be included within its capsule. They produce an internal secretion which helps regulate calcium metabolism and maintain the blood calcium at a level of from 9 to 11 mg. per 100 c.c.

Parathyroid hypofunction leads to a reduction in blood calcium. When the blood calcium falls to about 7 mg. per 100 c.c., tetany develops. Parathyroid hypofunction may be alleviated by the administration of parathyroid extract, but its use must be controlled by frequent determinations of the amount of blood calcium or else too much may be given. Unless parathyroid extract is given, complete removal of the parathyroid glands is quickly followed by tetany, ending in death. Their accidental removal was one of the causes of unexplained death in the early days of thyroid surgery.

Hyperparathyroidism is characterized by a high blood calcium and a marked rarefaction of bone with the development of cysts.

IV. THE PITUITARY BODY (HYPOPHYSIS)

A. Introduction

The pituitary body consists of an anterior lobe and a smaller posterior lobe which differ in development, structure, and function. The former is a glandular structure and the latter is of nervous origin.

The anterior lobe has at least seven functions, among which are (1) control of skeletal growth, (2) regulation of the action of the thyroid gland and, (3) influence on the metabolism of carbohydrates and fats. It secretes at least two hormones which have a maturing action on the Graafian follicles of the ovary. During pregnancy the amount of these hormones in the blood is increased and they escape into the urine. If the urine is injected into the body of a sexually immature animal, the hormones act on the Graafian follicles of the ovary and bring about their maturation. Upon this phenomenon are based the highly reliable *Aschheim-Zondek* and *Friedman* tests for pregnancy. In the former the white

mouse is used as the test animal and in the latter the rabbit is used.

The posterior lobe is the source of pituitrin which causes contraction of smooth muscle fibers, increases peristalsis, retards the flow of urine, slows the heart action, and raises the blood pressure. It is frequently used in obstetrics and surgery.

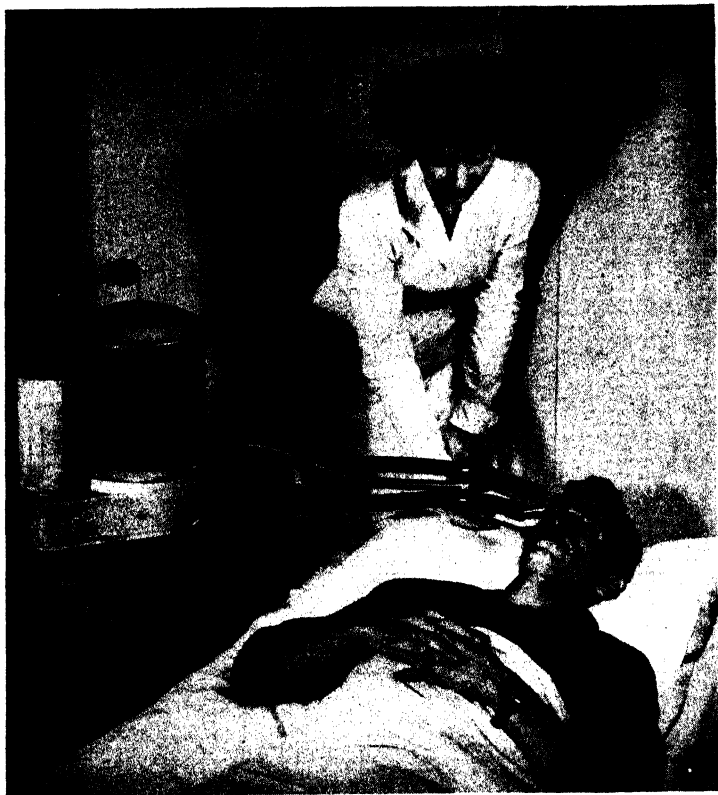


Fig. 211.—Technician performing a metabolism test. The patient breathes oxygen from the machine which records the amount of oxygen consumed. The consumption of a small, normal, or large amount of oxygen is indicative of a low, normal, or high state of metabolic activity. This test is of great value in the diagnosis of diseases of the thyroid gland. It also has other fields of usefulness.

Overfunction and underfunction of the pituitary body gives rise to *hyperpituitarism* and *hypopituitarism*, respectively.

B. Hyperpituitarism

Excessive activity of the anterior lobe of the pituitary body occurs in two forms: gigantism and acromegaly.

Gigantism.—In pituitary gigantism the person is abnormally tall due to an excessive length of the lower extremities. In some cases the hyperactivity of the anterior lobe is found to be due to the presence of a tumor. In most cases lesions of other endocrine glands are also present. Pituitary giants are often sexually impotent and frequently die of diabetes. Gigantism results when an excessive activity of the pituitary is congenital or sets in before ossification is complete.

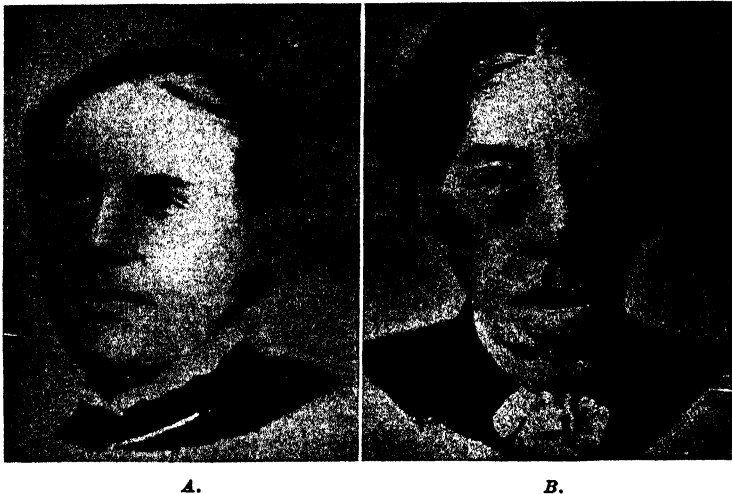


Fig. 212.—A, Appearance of patient who later developed acromegaly. B, Same patient seventeen years later. (After Campbell Geddes, from Bard: *Macleod's Physiology in Modern Medicine*.)

Acromegaly.—When anterior pituitary hyperactivity sets in after ossification is complete, the bones of the hands, feet, and lower jaw thicken and enlarge. The enlargement of the lower jaw gives rise to the highly characteristic “lion face” appearance. In addition there is considerable enlargement of the nose, lips, ears, and internal organs. Some degree of gigantism may also be present. Diabetes mellitus is often present. The mentality may be normal or impaired. After a period of time pituitary hyperfunction is followed by a loss

of function which is indicated by sexual impotence, drowsiness, and a tendency to become fat. As in gigantism, the hyperactivity of the anterior lobe is in some cases found to be due to the growth of a tumor.

C. Hypopituitarism

Hypoactivity of the anterior lobe of the pituitary may be due to tumor growths or other destructive lesions.

Dwarfism.—When there is a congenital absence or great diminution in the secretion of the anterior lobe of the pituitary body, dwarfism results. These dwarfs are usually deformed or have the appearance of being prematurely old.

Pituitary Cachexia.—On rare occasions, especially after childbirth, a general wasting away of the body occurs in women without apparent cause. In these cases there is often found a destructive lesion of the whole of the pituitary body or of its anterior lobe.

D. Diabetes Insipidus

According to many authors, diabetes insipidus is due to destructive lesions of the posterior lobe of the pituitary body. The disease is characterized by extreme thirst and the passing of large amounts of urine that does not contain sugar and is of a low-specific gravity. Some cases are relieved by the administration of pituitrin, which supports the belief that the disease is due to a deficiency of the posterior lobe of the gland.

V. THE ADRENAL GLANDS

The adrenal glands are two organs consisting of two portions, an outer zone (cortex) and a central portion (medulla), which differ in origin, structure, and function. The medulla produces *epinephrine*, or adrenalin as it is often called, which causes contraction of the blood vessels, raises blood pressure, and slows the heart. The output of epinephrine is increased by emotional disturbances such as anger, etc. Complete extirpation of both adrenal glands may be followed within one or two days by muscular weakness, great prostration, and low blood pressure, ending in death. or the patient may apparently recover from the primary

effect only to die at a later period in a state characterized by low blood pressure and a progressive muscular weakness which reaches a state of paralysis and ends in convulsions, coma, and death. Death in diphtheria, scarlet fever, and bacillary dysentery are, in part, due to adrenal failure. Those doing operations on the kidney should exercise caution lest they injure the adrenal gland. Extirpation experiments have shown that the cortex is the part of the gland that is essential to life and that such is not the case of the medulla. The cortex does not produce epinephrine.

Addison's Disease.—Addison's disease is a peculiar disease in which autopsy usually reveals a bilateral destructive lesion of the adrenal glands, most often tuberculosis. Some cases are probably due to syphilitic or neoplastic involvement of the glands.

The disease is most common in males who have reached the later years of life. It begins rather insidiously with digestive disturbances and loss of appetite. This is followed by vomiting, diarrhea, decrease in blood pressure, progressive emaciation and weakness, and a peculiar splotchy grayish brown pigmentation of the skin. After a time the patient becomes so weak that he takes to his bed, from which he never rises. The time elapsing between the onset of the disease and death is usually about a year. The disease seems to be due to a loss of function of adrenal, cortex, and medulla.

VI. THE THYMUS

The thymus is present at birth and continues to enlarge until puberty and then decreases in size. It has gained medical recognition because of its true or supposed relation to status lymphaticus.

Status Lymphaticus.—Status lymphaticus, or status thymicolymphaticus, is a condition in which there is an increase in the size of the lymph nodes and spleen, hyperplasia of other lymphoid tissue, smallness and weakness of the blood vessels and heart, persistence or enlargement of the thymus, and a tendency to sudden death from trivial causes such as anesthetics, slight blows, etc. The disease is most common

in males, and their bodies often resemble the female in form. Death is sometimes found to be due to cerebral hemorrhage. Deaths in which cerebral hemorrhage are not found have been attributed to an intoxication of an anaphylactic nature. Recent researches indicate that enlargement or persistence of the thymus does not have as an important causative relation to status thymicolymphaticus as was once accorded it.

VII. THE PANCREAS

Although we have found that the pancreas has an important external secretion, we must not forget that it has an important internal secretion that regulates carbohydrate metabolism. This secretion, known as *insulin*, is produced by the islands of Langerhans, and when the pancreas is so diseased that the islands cannot produce sufficient insulin, *diabetes mellitus* results. In this disease glucose is not stored within the body and oxidized as is normally the case but accumulates in the blood and escapes into the urine. Various lesions of the pancreas have been found in diabetes, but as yet no lesion has been found with sufficient frequency to be called *the* lesion of diabetes mellitus.

In diabetes mellitus carbohydrate metabolism may be restored to normal and all of the manifestations of the disease controlled by the administration of insulin. Its administration must be carefully controlled or overdosage may lead to a train of symptoms consisting of low blood sugar, weakness, fatigue, profuse sweating, mental disturbances, and convulsions. This is known as *hyperinsulinism*, which may be of gradual or sudden onset. It demands immediate treatment. Symptoms usually appear when the blood sugar falls to a level of 45 mg. per 100 c.c. of blood.

Questions for Review

1. What are the symptoms of myxedema?
2. What are the symptoms of hyperthyroidism?
3. What is Graves' disease?
4. Explain the basis for the Aschheim-Zondek and Friedman tests for pregnancy.
5. What are the symptoms of status lymphaticus?
6. Give the symptoms of hyperinsulinism.

True-False Test

Place the word "true" or "false" before each statement.

- 1. There is no interrelation existing between the endocrine glands.
- 2. According to several authors, diabetes insipidus is due to destructive lesions of the posterior lobe of the pituitary body.
- 3. Hypofunction of the adrenal glands gives rise to tetany.

Completion Test

- 1. The internal secretions have been classified as -----
- 2. Colloid goiters usually produce -----
- 3. Hyperplastic goiters usually produce -----
- 4. The thyroid gland, in part, controls ----- and ----- and exerts an influence on the ----- and -----
- 5. A congenital deficiency in thyroid secretion leads to ----- or -----
- 6. A carcinoma of the thyroid usually metastasizes to the ----- and -----
- 7. Parathyroid hypofunction leads to a reduction in ----- and the disease known as ----- develops.
- 8. Excessive activity of the anterior lobe of the pituitary body occurs in two forms: ----- and -----
- 9. Hypoactivity of the anterior lobe of the pituitary results in -----

References

- Bard, Philip, and Collaborators: *Macleod's Physiology in Modern Medicine*, St. Louis, 1941, The C. V. Mosby Co.
- Joll, Cecil A.: *Diseases of the Thyroid Gland*, St. Louis, 1940, The C. V. Mosby Co.
- Anderson, W. A. D.: *Synopsis of Pathology*, St. Louis, 1946, The C. V. Mosby Co.

CHAPTER LIX

DISEASES OF THE BONES AND JOINTS

I. THE BONES

A. Inflammations

Inflammation of the bone may primarily involve the cancellous bone and marrow, compact bone or periosteum, giving rise to *osteomyelitis*, *osteitis*, and *periostitis*, respectively. In most cases the inflammation spreads from the primary focus until cancellous bone, marrow, compact bone, and periosteum are all involved.

It should be remembered that the underlying mechanism of inflammation in bone is in no manner different from that of inflammation in other tissues, the difference in results being due to the peculiar structure of bone. Pyogenic infections of the bones seldom involve the joints because the epiphyseal cartilage, which usually lies between the joint and the site of infection, acts as a barrier. This is the direct opposite of tuberculosis in which infection of the bone usually spreads to the joints.

Acute osteomyelitis is most often due to bacteria that have been carried to the cancellous bone or marrow by the blood stream. The bacteria may be deposited during the course of a septicemia, or may be brought from such distant foci as infected teeth or tonsils. In some cases it may be due to the ingress of bacteria from the periosteum or their introduction by gunshot wounds, compound fractures, amputations, etc. Infections of the middle ear often spread to the mastoid process and cause a fulminating osteomyelitis. Staphylococci and streptococci are the organisms most often responsible for acute osteomyelitis.

Acute osteomyelitis begins most often in the end of a long bone, especially the upper end of the tibia or the lower end of the femur. From the point of origin the infection may spread along the cavity of the bone until the whole shaft becomes filled with purulent material, and it may spread by the blood and lymph to the periosteum. In some cases the

exudate breaks through the bone and produces a cellulitis that discharges on the surface. In fulminating cases of osteomyelitis the joint may be involved, but in most cases the epiphyseal cartilage protects the joint against invasion. Acute fulminating osteomyelitis is a most serious condition and often terminates fatally.

When a bone becomes infected the bacteria may remain for years and give rise to a *chronic osteomyelitis* with recurrent more or less acute attacks. A typical example is the chronic osteomyelitis due to *Bact. typhosum*, which may begin a month or two or years after an attack of typhoid fever.

B. Tuberculosis

Tubercle bacilli may reach the bones from distant foci via the blood stream or by direct extension from a joint.

Tuberculosis of the bones is most common in childhood. It usually begins in the cancellous tissue of the vertebrae or in the ends of the long bones, particularly the tibia and femur. The disease is primarily an osteomyelitis.

At first one or more tubercles are formed and other tubercles are then formed around them. Very small areas may become encapsulated and larger ones may become separated from the healthy bone, forming a sequestrum, but usually the focus gradually softens and forms a tuberculous abscess. Extension to the adjacent joint often occurs, and the process may spread along the medullary cavity of long bones to involve the whole of their shaft, with the production of an abscess that discharges on the surface. When the disease spreads in this manner a large amount of bone is destroyed, and the periosteum is stimulated to form osseous tissue which leads to great enlargement and expansion of the bone. Since tuberculosis of the bone often extends to the joint and vice versa, bone and joint tuberculosis are often associated. Tuberculosis of the hip joint is one of the common surgical diseases of childhood.

Tuberculosis of the Spine (Pott's Disease).—Tuberculosis of the spine is primarily a disease of childhood but may occur in adults. The vertebrae most often involved are the last three dorsal and first two lumbar. As a rule, two or

more vertebrae are involved. In children the centers of the vertebrae are primarily attacked, and in adults the periphery is primarily attacked. When the central portion is attacked, the bone is destroyed and replaced by granulation tissue, which becomes converted into a softened caseous material.



Fig. 213.—Pott's disease of the spine. (From Boyd, William: *Surgical Pathology*. W. B. Saunders Co.)

Finally the affected vertebrae are crushed by the weight which they support, and this brings about an anterior curvature of the spinal column. When the peripheral portion of the bone is attacked, there is not so much bony destruction and the deformity is less.

Tuberculous pus has a remarkable tendency to burrow, and the pus from tuberculous vertebrae may approach the surface at a considerable distance from the diseased bone, the point of approach depending to a great extent on the location of the involved vertebrae. In tuberculosis of the cervical

vertebrae the pus may collect between the vertebral column and the posterior pharyngeal wall, forming a retropharyngeal abscess. In the vertebra of the dorsal region the pus may enter the sheath of the psoas muscle, forming a psoas abscess which may reach the surface in the lumbar region, or groin. An abscess coming to the surface in the groin may be mistaken for a hernia.

C. Syphilis

The lesions of early congenital syphilis may be present at birth or may appear later. The most characteristic lesion is an osteochondritis affecting the area of growth between the diaphysis and epiphysis of the long bones, but any bone may be involved. Since the osteochondritis interferes with growth, the bones do not reach their normal length; the epiphyses may become separated from the shafts of the bones, and the child may be unable to walk. The tibia may be thickened and curved forward, forming the so-called "saber blade" tibia. The destructive action of gummas of the nasal bones and palate may give rise to saddle nose and perforation of the palate. Gummas of the skull are not infrequent, and bossing of the skull and craniotabes are common.

In late congenital syphilis and acquired syphilis the periosteum is most often involved, but the medulla of the bone may be affected. The joints are seldom affected. The periosteal involvement usually takes the form of a periostitis, but gummas may occur. The shin bones are most often affected. When the involvement takes the form of a periostitis, the formation of bony nodules gives the shins a roughened, uneven appearance. The involvement of the underlying bone is more extensive in gummas of the periosteum than in periostitis. In either case extensive rarefaction or sequestrum formation may occur.

D. Tumors

1. **Introduction.**—Tumors of the bones may be benign or malignant. The latter may be primary or metastatic. Primary malignant tumors of bone are most often of a sarcomatous nature. Metastatic tumors of bone are most often of a carcinomatous nature.

2. Benign Tumors.—The most important benign tumors of bone are osteomas, chondromas (tumors derived from cartilage), fibromas, myxomas, and giant cell tumors.



Fig. 214.—Osteosarcoma involving the marrow of the humerus, piercing the cortex in many places, and growing out radially under the periosteum. (From MacCallum: *A Textbook of Pathology*. W. B. Saunders Co.)

OSTEOMAS.—Osteomas are benign tumors composed of bone. They are comparatively rare. It is often difficult to differentiate true osteomas from certain common bony overgrowths due to injuries or inflammatory conditions. Among the latter are calluses (which form at the site of fractures), exostoses, and endostoses.

True osteomas usually occur in connection with the bones of the face, most often in the nasal sinuses or orbit. Other tumors sometimes undergo secondary ossification. This is most common in fibromas, lipomas, and certain sarcomas.

GIANT CELL TUMORS.—These tumors are often called giant cell sarcomas which is incorrect because the term “sarcoma” indicates a highly malignant tumor while the tumor under consideration is comparatively benign. Some workers believe that these growths represent a peculiar reaction to some inflammatory condition and are not tumors at all. Giant cell tumors most often affect the lower jaw where they are known as *epulides* (plural of *epulis*), but they may occur in other locations, notably the ends of long bones. Giant cell tumors of the ends of the long bones are not quite as benign as giant cell tumors of the jaw. The growth usually arises from the periosteum and forms a firm, slowly enlarging mass, but in a few cases it arises in the medullary portion of the bone and is soft and jellylike in consistency. *Epulis* is of the former type. As a rule, giant cell tumors require no treatment other than local excision.

Giant cells tumors should not be confused with certain rather highly malignant sarcomas that contain giant cells. The giant cells of the former are of the foreign body type. Those of the latter are true tumor cells.

3. Primary Malignant Tumors.—Osteogenic sarcoma, Ewing's tumor, myeloma, and extraperiosteal sarcoma are the most important primary malignant tumors of the bones. Extraperiosteal sarcoma is a comparatively rare tumor that is not a true bone tumor because it arises from the periosteal connective tissue and does not form bone. The causative relation between traumatism and tumor growth seems to be more definitely established in bone tumors than in tumors arising from other tissues. However, bone tumors seldom follow such extensive injuries as fracture, etc.

4. Metastatic Tumors of Bone.—The important metastatic tumors of bone are carcinomas and hypernephromas. The most important metastatic carcinomas are those arising from the breast, thyroid gland, stomach, and genitourinary organs, especially the prostate. The bones most often affected are

the vertebrae, ribs, sternum, skull, pelvis, femur, and humerus. The cancellous portion of the bone is primarily attacked. Hypernephromas often metastasize to the skull. Pain, swelling, or fracture of a long bone frequently calls attention to a metastatic tumor before the primary tumor has been discovered. A metastasis of a cancer of the prostate is always to be thought of when an elderly man has a spontaneous fracture. A widespread carcinomatous involvement of the bone marrow may lead to a profound anemia.

II. THE JOINTS

A. Acute Arthritis

Acute arthritis (inflammation of a joint) may be of infectious or noninfectious origin and may be suppurative or non-suppurative. One or many joints may be involved. Acute arthritis of infectious origin may be due to streptococci, staphylococci, or pneumococci or, less often, to other bacteria. One of the less common causes of acute arthritis is the gonococcus, but in many cases gonorrheal arthritis is of a more chronic than acute nature. In infectious arthritis the causative bacteria may reach the joint through penetrating wounds or by extension from a nearby site of infection, most often the end of one of the bones composing the joint, but in the majority of cases they are conveyed to a joint or joints by the blood stream. Arthritis of blood stream origin is a characteristic feature of acute rheumatic fever and may occur during the course of septicemia, subacute bacterial endocarditis, and certain infectious diseases, especially pneumonia, scarlet fever, typhoid fever, epidemic meningitis, undulant fever, and bacillary dysentery. In some cases the bacteria apparently are carried to the joints by the blood stream from distant foci or more or less chronic infection, such as boils, infected sinuses, abscessed teeth, and inflamed tonsils. Noninfectious arthritis may be due to injuries of the joints or it may be of allergic origin.

In a few cases of purulent arthritis recovery with a fairly useful joint occurs, but in most cases the destruction of tissue is so great that the reparative processes lead to so many fibrous, cartilaginous, or bony adhesions that the joint is

left in a state of ankylosis. In a not inconsiderable number of cases the patient dies from toxemia or septicemia during the acute stages of the disease.

A rare but peculiar condition of the joints is *intermittent hydrarthrosis*, which usually affects the knee joint and is characterized by periodic attacks of effusion into the joint, which occur at regular intervals, most often every ten or eleven days. Its cause is not known, but there is some evidence that it is of allergic origin.

B. Chronic Arthritis

Most workers include within the term chronic arthritis any chronic inflammation of the joints except tuberculosis and syphilis, and we will adhere to that plan.

In the absence of exact knowledge of its etiology a satisfactory classification of chronic arthritis is difficult and must be made on the basis of the clinical manifestations of the disease and the structural changes occurring in the affected joints. Probably the most satisfactory classification is into chronic infectious arthritis and osteo-arthritis. In chronic infectious arthritis several joints are usually involved; the disease begins in the capsule of the joint and often leads to ankylosis. In osteo-arthritis a single joint is often involved, the articular cartilages are primarily attacked, and the disease leads to cartilaginous and bony overgrowths but not to ankylosis.

1. Chronic Infectious Arthritis.*—Chronic infectious arthritis is the most common type of chronic arthritis and occurs most often in women between twenty and forty years of age, but it may occur in children. It is infrequent in adult males. As a rule, several joints are involved, but in rare instances the disease may be confined to a single joint. This disease is characterized by its progressive course, and it may lead to such deformity and interference with function that the patient is rendered hopelessly deformed and crippled for life.

*Chronic infectious arthritis is also known as rheumatoid arthritis and arthritis deformans. Some investigators consider rheumatoid arthritis a bad term, because they believe there is no relation between chronic infectious arthritis and rheumatic fever, while others regard the two diseases as different manifestations of the same underlying cause. Some authors prefer to include any type of arthritis that is accompanied by marked deformity and crippling under the term "arthritis deformans." Osteo-arthritis is known also as degenerative arthritis.

Considerable evidence indicates that chronic infectious arthritis is due to an attenuated streptococcus, and in many cases the organisms can be found in the infected joints, but as yet the evidence is not entirely conclusive. The disease often follows severe physical strain, injuries, exposure to bad weather, and in many cases a hereditary factor seems to be present. Many patients give a history of antecedent infections, such as infections of the teeth, throat, genitourinary organs, appendix, and gallbladder. Chronic infectious arthritis is characterized by its progressive nature and its tendency to produce deformity and ankylosis of the joints.

2. Osteo-arthritis.—Osteo-arthritis differs from chronic infectious arthritis in that it (osteo-arthritis) is a degenerative rather than an inflammatory condition, is more common in males than in females, occurs most often in middle life and old age, affects fewer joints (often being confined to a single joint), and is not followed by ankylosis.

The exact cause of osteo-arthritis is not known. In some cases it follows an injury. It has been suggested that there is some relation existing between osteo-arthritis and arteriosclerosis because patients who develop osteo-arthritis often have arteriosclerosis. Arteriosclerosis, however, is a common disease, and by the law of chance a number of people who have osteo-arthritis would also have arteriosclerosis. In addition to arteriosclerosis, evidences of advancing years that are often associated with osteo-arthritis are obesity and gray and falling hair.

C. Gonorrheal Arthritis

Gonorrheal arthritis formerly complicated or followed from 2 to 5 per cent of cases of gonorrhea, but since the advent of the sulfonamide drugs it has become a rather rare disease. It usually begins near the end of the third week of the disease but may occur months after the acute manifestations of the disease have subsided. Gonorrheal arthritis occurs more often in men than in women and usually affects the larger joints, especially the knee. Less often attacked are the ankle, wrist, shoulder, and elbow. As a rule, only a few joints are attacked, and in many cases the

infection is confined to a single joint. In some cases of polyarticular gonorrheal arthritis all of the joints except one return to normal, leaving a monarticular arthritis. Gonorrheal infections other than urethritis may be a source of gonorrheal arthritis. Injury of a joint during the course of a gonorrhea predisposes that joint to gonorrheal arthritis.

Gonorrheal arthritis may be acute or chronic. Acute gonorrheal arthritis often begins suddenly with chilly sensations or distinct chills, swelling of the affected joint or joints, intense pain, and fever.

The most common type of acute gonorrheal arthritis is characterized by a serofibrinous exudate into the joint. The joint is red, swollen, and painful. This type of gonorrheal arthritis is more likely to be polyarticular than the others. It may end by resolution or may progress to chronic arthritis with hydrops or, more rarely, may end in suppuration. Suppurative gonorrheal arthritis is characterized by high fever and severe constitutional symptoms, with marked pain and destruction of joint tissue that may lead to ankylosis.

Chronic hydrops of gonorrheal origin is comparatively painless and usually begins insidiously, but it may follow an acute gonorrheal arthritis. Most often it is monarticular and attacks one of the larger joints. Ordinarily constitutional symptoms are absent. Chronic hydrops may end spontaneously or resist all forms of treatment.

Gonorrheal inflammation of the bursa between the Achilles tendon and the os calcis or gonorrheal inflammatory exostoses may give rise to extreme pain in the foot.

D. Tuberculous Arthritis

Tuberculosis of the joints is usually due to the extension of a tuberculous process from an adjacent end of one of the bones of the joint, but in some cases it begins as a primary process in the synovial membrane without involvement of the bone. The latter mode of origin is most common in adults. The focus in the bone or synovial membrane may be secondary to some other focus, such as a pulmonary tuberculosis or tuberculous adenitis, but in many cases such foci cannot be

detected. Injury to a joint seems to render it more susceptible to the invasion of tubercle bacilli.

Tuberculous arthritis usually occurs before the sixth year of life, but no age is exempt. As a rule, the infection is confined to a single joint, and the joints most often affected in order of frequency are the hip, knee, elbow, shoulder, and ankle. Excluding tuberculosis of the spine, tuberculosis of the hip is more common than tuberculosis of all other joints combined. It is one of the common surgical conditions of childhood.

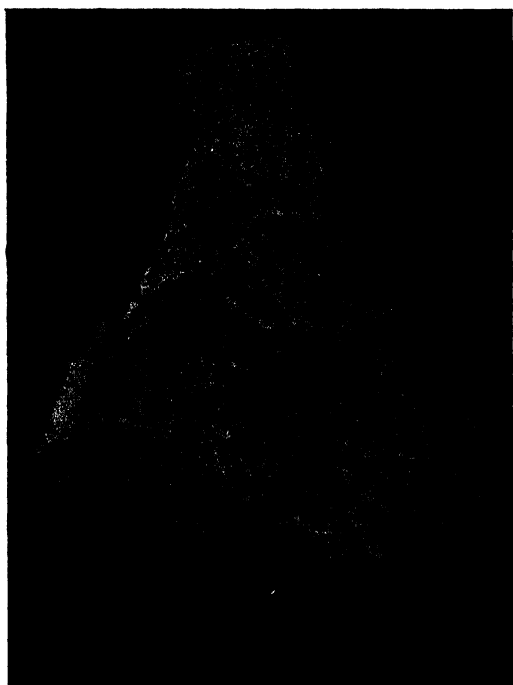


Fig. 215.—Tuberculosis of lower end of tibia. (From Boyd, William: *Surgical Pathology*. W. B. Saunders Co.)

When the arthritis is due to the extension of a tuberculous process from the adjacent bone, any part of the joint may be attacked, but the synovial membrane is ultimately involved and foci beginning in the synovial membrane finally destroy the articular cartilages and invade the bone. When extensive

destruction of the soft parts of the joint has occurred, the joint assumes a spindle shape and may become partially dislocated. The overlying muscles and skin undergo a gelatinous degeneration which gives the skin a white appearance and causes one or more veins to stand out prominently. This is known as "white swelling."

Although a spontaneous cure may occur in all but the more advanced cases of tuberculous arthritis, such is not the usual outcome, and surgery has to be resorted to in order to effect a cure. Even then the patient is often left with a stiff or completely ankylosed joint. Secondary infection of the sinuses leading from a tuberculous joint may lead to suppuration within the joint cavity. Amyloid infiltration of the liver, spleen, and kidneys may follow long-standing cases. As a whole the outlook is better in children than in adults.

E. Syphilis of the Joints

Syphilis of the joints may occur in either congenital or acquired syphilis, and in the latter it may occur in either the secondary or tertiary stage.

The joint manifestations of secondary syphilis are not of a destructive nature, and the only symptom may be rheumatic pains that are worse at night and are not aggravated by motion. In most cases, however, there is moderate tenderness, swelling of the joint, and limitation of motion. The knees are most often affected and the condition is frequently bilateral. In the late secondary stage the joints may become markedly distended, producing a condition that is cured with difficulty.

In tertiary syphilis there is most often a gummatous or diffuse inflammatory infiltration of the synovial membrane, and the articular ends of the bones may be affected. The affection is usually monarticular and the knee joint is most often involved. There is considerable swelling but no redness of the joint.

Congenital syphilis of the joints may occur in the form of syphilitic epiphysitis in infants or syphilitic synovitis in older children and young adults. In the former the involve-

ment of the epiphysis leads to swelling, tenderness, and pain in the joint. Separation of the epiphysis may occur. In syphilitic synovitis the knee is most often affected, and the condition is usually bilateral. It may take the form of a simple effusion or gummatous synovitis.

Questions for Review

1. Define: osteomyelitis, osteitis, periostitis.
2. What organisms are most often responsible for acute osteomyelitis? How do they reach the bones? What portion of the bone is most often the site of origin of an osteomyelitis? What bones are most often involved?
3. How do tubercle bacilli reach the bones? Is the joint more likely to be involved in tuberculosis of the bone than in a more acute inflammation? Why?
4. What is Pott's disease? How does it differ in children and adults?
5. What is a psoas abscess? Where may a psoas abscess point?
6. Give some of the causes of acute arthritis.
7. Discuss tuberculous arthritis.
8. Discuss syphilis of the joints.

References

- Boyd, William: Surgical Pathology, Philadelphia, 1947, W. B. Saunders Co.
- Ewing, James: Neoplastic Diseases, Philadelphia, 1940, W. B. Saunders Co.
- Foot, N. Chandler: Pathology in Surgery, Philadelphia, 1945, J. B. Lippincott Co.
- Geschickter and Copeland: Tumors of Bone, New York, 1936, The American Journal of Cancer.

PART III

LABORATORY EXERCISES

I. EXERCISES IN MICROBIOLOGY

The following exercises are designed to serve as a guide to be followed in demonstrating to the student some of the fundamentals of microbiology. They may be varied to meet the needs of the individual student and to fit the teaching facilities of the school. As far as possible, details of technic have been omitted because it is our view that much confusion will be avoided if the student is taught the details of technic to which the instructor is accustomed. In all cases the exercises have been designed so as to be carried out with a minimum of equipment and without undue labor or danger on the part of the student.

GENERAL LABORATORY RULES

In order that laboratory work may be of the highest quality and that students may not endanger themselves or others, certain laboratory rules must be followed. Important among these rules are the following:

1. Disinfect hands and desk at beginning of laboratory period.
2. Wear laboratory coat or jacket.
3. Avoid spilling material on desk or floor. If infectious material comes in contact with desk or floor, disinfect at once.
4. All cultures or infectious material must be disposed of in such a manner as to be of no danger.
5. Glassware and other equipment should be kept clean and in its proper place.
6. The microscope should be properly cared for.
7. The student should provide himself with a notebook and keep an accurate record of each experiment. Included in the notes on each experiment should be (1) the purpose of the experiment, (2) how it was performed, (3) the results obtained, and (4) the conclusions reached. The

notebook should be neatly kept and should be corrected at frequent intervals by the instructor.

8. Disinfect hands and top of desk before leaving the laboratory.

EXERCISE 1. THE MICROSCOPE

Reference: Chapter III

1. Locate all parts of the microscope labeled in Fig. 8. By means of their numbers, locate the low power, "high dry," and oil immersion objectives. Observe movements brought about by manipulating coarse and fine adjustments.
2. With the aid of the instructor, focus low power objective on some large object; for instance, on a section of tissue. Observe change in lighting brought about by changing position of mirror and opening and closing iris diaphragm. When you have the field evenly and properly lighted, have the instructor see if the lighting can be improved.
3. In the same manner focus the high dry lens.
4. Under the direct supervision of the instructor, focus the oil immersion lens.
5. Calculate the magnification of the different objectives of your microscope with each eyepiece.
6. Solve the problem given with Fig. 9.
7. Under the supervision of the instructor, clean your microscope and return it to your locker.

EXERCISE 2. THE CELL

Reference: Chapter IV

1. Place a drop of water on a clean glass slide. Mount a piece of the membrane separating the inner layers of an onion in the water. Place a cover glass on the preparation and gently press down. Remove excess of water from slide with clean cloth. With the low power of the microscope sketch a small group of cells. With the high dry objective sketch a single cell.
2. With a razor blade or sharp scalpel cut a very thin slice of potato. Mount as outlined in experiment 1. Examine

under low power of microscope and with high dry objective. Note starch granules. Remove cover glass and add a drop of iodine solution to the preparation. Replace cover glass and examine as before. What change has taken place?

3. Scrape the inner surface of the cheek with the blunt edge of a scalpel. Mount the scrapings in a drop of water and apply cover glass. Examine with low power of the microscope. With the high dry objective sketch a few epithelial cells which may be recognized by their "pavement" appearance. They may occur singly or in clusters. Locate any blood cells or bacteria that may be present.
4. Mount scrapings from inside of cheek as outlined in experiment 3, but spread into a thin even smear with a toothpick instead of covering with a cover glass. Let dry and pass rapidly through a flame two or three times to "fix" the smear. Cover smear with methylene blue stain and allow to remain for three minutes. Wash stain off with distilled water. Blot between sheets of blotting paper. Examine with oil immersion objective. Sketch three or four cells. Show relation existing between nucleus and cytoplasm.
5. Place a drop of centrifugalized urine on a slide and cover with a cover glass. Examine with low power of microscope and high dry objective. Look for epithelial cells and leucocytes. Make a sketch showing the different objects seen. With the aid of the instructor identify them.
6. **Preparation and Examination of Blood Smears:**
 - a. *Obtaining the Blood.*—In this experiment students may work in pairs but after the blood has been obtained each student should work individually. Cleanse end of finger with alcohol and remove alcohol with dry cotton. With a sterile needle prick end of finger with enough force to get a good drop of blood. Gently squeeze finger until blood exudes.
 - b. *Making the Smear.*—Touch clean slide to drop of blood on finger. The drop of blood should be about 1.5 cm.

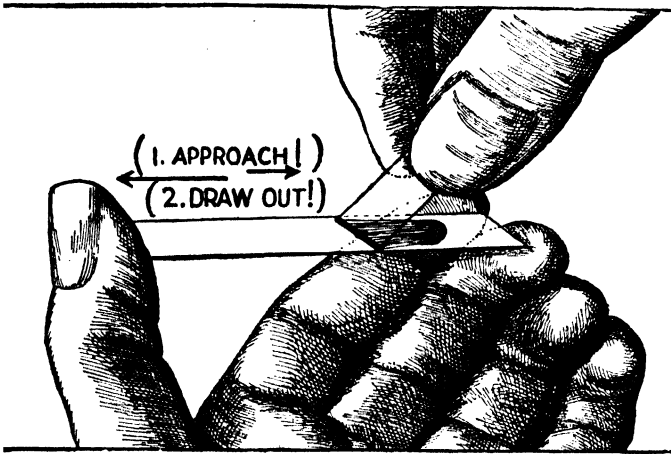


Fig. 216.—Method of making a blood smear. Compare with Fig. 34, page 100. (From Schilling: The Blood Picture.)

from one end of slide. Place the slide on a level surface with the drop of blood up. With one hand steady the slide and with the other place the end of another slide which acts as a "spreader" flat against the surface of the blood slide so that an angle of about 45° is formed. Draw spreader slide back until its edge comes in contact with the drop of blood. Let the blood spread along junction of the two slides. Push spreader slide forward. The thickness of the smear will depend on the acuteness of the angle and the rapidity with which the slide is pushed along.

- c. *Staining the Smear.*—After the smear has dried in the air cover with Wright's stain and let stand $\frac{1}{2}$ to 1 minute. Without removing any stain add about twice as much distilled water as stain. Let remain until a metallic scum forms (usually 2 to 3 minutes). Wash with distilled water and dry between sheets of blotting paper.
- d. *Examination.*—Examine with the low power of the microscope and oil immersion objective. Red cells appear pink. Those from normal adult human blood do not contain nuclei. White cells have dark blue nuclei with light blue or purple cytoplasm. Sketch a few red cells; a few white cells. From your study of this slide do you think that there are different types of red blood cells or are all essentially alike? How would you answer this question when applied to white blood cells?
7. Examine a prepared smear of pus. Use oil immersion objective. Sketch a few pus cells. From your study of this slide and the previous exercises draw some conclusion regarding the origin of pus cells.
8. The instructor will furnish you with slides showing the primary tissues (epithelium, connective tissue, muscle tissue, nerve tissue). Make a sketch of a few fibers of each.
9. Examine a hay infusion that has stood for several days. An actively motile protozoon (paramecium) should be found.

EXERCISE 3. GENERAL CHARACTERISTICS OF BACTERIA

Reference: Chapter V

1. *Distribution of Bacteria:* In this experiment students should work in groups of two. Each group is furnished four Petri dishes. One Petri dish is exposed for five minutes in the laboratory; another for the same length of time just after the laboratory has been swept. The third and fourth are exposed in selected locations such as the nurse's bedroom, ward, kitchen, etc. Exposure is made by removing the lid from the dish. Do not invert the lid. Replace lid and place dish, bottom up, in incubator for 24 to 48 hours. Wherever a bacterium comes in contact with the surface of the medium a "colony" will develop. Does plate 1 or 2 have more colonies? What does this indicate? How does the number of colonies on plates 3 and 4 compare with the number on plates 1 and 2? Are all colonies alike or do they differ in such characteristics as size, shape and color? What does this indicate?
2. The student should examine and make drawings from the following prepared slides showing the shape of bacteria: (1) cocci, (2) bacilli, (3) spirilla.
3. Students should examine and make drawings from prepared slides showing the following arrangements of bacteria: (1) staphylococci, (2) diplococci, (3) streptococci and (4) streptobacilli.
4. Students should examine and make drawings from prepared slides of bacteria showing the following structures: (1) spores, (2) capsules, (3) metachromatic granules, and (4) flagella.
5. Motility of bacteria as observed in hanging drop preparations should be demonstrated by the instructor. He should briefly discuss the technic of preparing hanging drop preparations.
6. The instructor should inoculate several large tubes of broth with different species of bacteria. One tube should remain uninoculated and serve as a control. Students

should examine tubes every few hours to determine presence or absence of bacterial multiplication, which will be indicated by turbidity of the broth.

EXERCISE 4. CONDITIONS AFFECTING GROWTH OF BACTERIA

Reference: Chapter VI

1. *Influence of Temperature on Bacterial Growth.*—The instructor will furnish you three broth cultures immediately after their inoculation. Note that all are clear because bacterial growth has not occurred. Place one in the ice-box, another at room temperature and another in the bacteriological incubator. Observe at end of 24 hours. In which tube is the growth, as indicated by cloudiness, most abundant? What does this prove?
2. *Effect of Reaction of Medium on Bacterial Growth.*—The instructor will furnish you five recently inoculated tubes of broth. Make additions to four of them as follows: (1) 0.2 c.c. N/1 NaOH, (2) 0.5 c.c. N/1 NaOH, (3) 0.2 c.c. N/1 HCl, (4) 0.5 c.c. N/1 HCl. The fifth serves as a control. Incubate at 37.5° C. for 24 hours. Compare the multiplication of bacteria in the different tubes as indicated by clouding of the medium.
3. *Effects of Sunlight on Bacterial Growth.*—The instructor will furnish you a recently inoculated Petri dish. Invert and cover one-half of the Petri dish in such a manner that direct sunlight is not allowed to strike the surface of the medium. Expose to sunlight for several hours. Incubate at room temperature until colonies appear. On which half of the plate are the colonies more numerous? What does this prove?

EXERCISE 5. SPECIAL ACTIVITIES OF BACTERIA

Reference: Chapter VII

1. The instructor will furnish you three Smith fermentation tubes. One contains 10 per cent dextrose solution; the second contains 10 per cent milk sugar solution and

the third contains a 10 per cent solution of cane sugar. Rub up a small piece of yeast cake in water and add a portion to each tube. Set in a warm place and observe at the end of 24 hours. What differences are noted?

2. *Prove that the gas formed in experiment 1 is carbon dioxide by the following technic:* measure the length of the gas column in the arm of the fermentation tube. (Remove a small amount of material from bulb of tube with pipette and reserve for experiment 3.) Fill bulb of tube with 10 per cent potassium hydroxide. Place thumb over mouth of tube and mix by inverting so that gas in arm of tube comes in contact with KOH. Collect all remaining gas in arm of tube. A reduction in the amount of gas proves that CO_2 was present and was absorbed by the KOH: $2\text{KOH} + \text{CO}_2 = \text{K}_2\text{CO}_3 + \text{H}_2\text{O}$.
3. *To prove that the fermentation in experiment 1 produced alcohol:* filter the liquid removed in experiment 2; to the filtrate add a few drops of weak iodine solution. Add enough 10 per cent sodium hydroxide solution to change the color from a brown to a distinct yellow. Warm slightly. A distinct odor of iodoform will be obtained and a yellow precipitate, appearing under the microscope as small hexagonal crystals, will be formed. If the amount of alcohol is small the crystals may not appear until the solution has cooled or stood some time.
4. *Fermentation with Acid and Gas Formation.*—The instructor will furnish you a phenol red dextrose broth fermentation tube recently inoculated with *Bact. coli*. Incubate 24 to 48 hours. Note multiplication of bacteria as indicated by turbidity. What other two changes have taken place? What does each indicate?
5. *Fermentation Causing Reduction of Pigment.*—Nearly fill a long narrow test tube with milk. Add enough weak aqueous solution of methylene blue to give the milk a distinct blue color. Add a little milk that has soured naturally. Mix and incubate at 37.5°C . for several days. What change has taken place?
6. The instructor will furnish you with three agar slants. One has been inoculated with *Ps. pyocyanea*, another with

B. prodigiosus and the third with *Staphylococcus aureus*. Incubate at 37.5° C. until pigment production is well developed. What color is produced by each? Is the color confined to the growth of bacteria or does it diffuse into the medium?

7. Examine cultures of *Staphylococcus albus*, *Staphylococcus citreus* and *Staphylococcus aureus*. What color is produced by each?

EXERCISE 6. METHODS OF STUDYING BACTERIA

Reference: Chapter VIII

1. The instructor will furnish you a broth culture of a motile organism. Make a hanging-drop preparation according to the method described on page 97, being careful to sterilize platinum loop in flame each time before and after it is used. Examine with high dry objective of microscope. The amount of light passing through the substage condenser must be somewhat reduced by partly closing the diaphragm. A properly made preparation shows the cells to stand out distinctly against a dully lighted background. Discard preparation according to method given by instructor. Why is this of importance?
2. Make hanging-drop preparation of a suspension of carmine. Note Brownian motion.
3. Make hanging-drop preparation of nonmotile organisms. Note that organisms do not change their position in relation to each other. Note Brownian motion.
4. The instructor should demonstrate the use of the dark-field microscope.
5. Make three smears, according to directions on page 99, of organisms furnished by instructor. Do not neglect proper sterilization of platinum loop.
6. After the smears have been "fixed," pour a few drops of methylene blue on the first, a few drops of gentian violet on the second, and a few drops of carbol-fuchsin on the third. Let stains act for one minute. Wash stains off with distilled water and drain slide. Blot

with blotting paper. Examine with oil immersion lens. Make drawings. What is the color of the organisms in each smear?

7. Place a loopful or two of a broth culture or watery suspension of bacteria on a slide. Add an equal amount of commercial India ink that has been diluted with two parts of water. Mix thoroughly and spread out slightly. Allow to dry and examine with the oil immersion objective. In satisfactory portions of the smear the bacteria stand out as colorless bodies against a gray-brown or black background. This is known as "relief" staining; i.e., the background is stained but the bacteria are not.
8. Make Gram stain of fixed smears furnished by instructor. Follow technic outlined on page 102. Are the organisms in the smear furnished you gram-positive or gram-negative?
9. Stain prepared and fixed slides of sputum furnished by instructor for *Myco. tuberculosis*. What method of staining are you going to use? What color is *Myco. tuberculosis* when stained by this method? Sketch one or two bacilli.
10. Make a methylene blue stain of a spore-forming organism. Note spores which appear as unstained areas in the cell body. Make drawing.
11. Make a Gram stain of pneumococci. Note the capsules which stand out as an unstained halo around the cell. Make drawing.

EXERCISE 7. THE STUDY OF BACTERIA BY CULTURES AND ANIMAL INOCULATION

Reference: Chapter IX

1. *Preparation of Culture Media*.—The instructor should demonstrate the steps taken in the preparation of two simple culture media, one liquid, the other solid. The purpose of different ingredients should be explained. The methods of adjusting the reaction of culture media should be demonstrated and the reasons why the reaction must be adjusted should be explained. Tubing and sterilizing the medium should be demonstrated. With a

portion of the solid medium which has been reserved, Petri dishes should be prepared. The method of incubating Petri dish cultures should be demonstrated.

2. After the instructor has demonstrated the method, students should make cultures from the throats of each other, using Loeffler's blood serum medium. Observe cultures at the end of twenty-four hours. Before this experiment the instructor should stress the purpose and necessity of flaming the mouth of culture tubes when making cultures or transfers.
3. The instructor should demonstrate different cultures on tubes of solid media and on "plates," i.e., Petri dish cultures. The differences in size, shape and contour of colonies should be demonstrated. Difference in ability of different organisms to grow on various media should be discussed.
4. Each student is furnished a culture of a nonpathogenic organism. After a demonstration of the method by the instructor, the students should transplant the organisms to fresh media. Incubate 24 to 48 hours.
5. Working in small groups the students should prepare pure cultures from a mixed culture furnished by the instructor. Use the "pour plate" method given on page 114.
6. The instructor will furnish you three Petri dishes of media. After reading the paragraph on streak plates and examining Fig. 41, page 117, prepare streak plates. Incubate 24 to 48 hours. Describe the plates. How does the distribution of the colonies on streak and pour plates differ?
7. The instructor should demonstrate how colonies are transferred from Petri dishes to agar slants. Why is it often necessary to do this?
8. *Counting Bacteria by Plating.*—During this experiment the students should work in small groups. Each group is furnished:
 - (1) A small amount of milk.
 - (2) Four tubes containing 9 c.c. sterile distilled water.

- (3) Five sterile 1 c.c. pipettes.
- (4) Four sterile Petri dishes.
- (5) A flask of melted agar that has been cooled to 42° C. Each flask should contain about 60 c.c. of agar and should be held at 42° C. in the water bath.

Procedure: Transfer 1 c.c. milk to a tube of distilled water and mix. With a fresh pipette transfer 1 c.c. of the mixture to a second tube of distilled water. Continue in this manner until the fourth tube is mixed, being careful to use a fresh sterile pipette to make each mixture. You now have 1:10, 1:100, 1:1,000, and 1:10,000 dilutions of milk. With a sterile pipette transfer 1 c.c. of each dilution to a Petri dish. Begin with the highest dilution and go to the lowest when making transfers. The material is transferred to the Petri dishes by slightly raising the lid and depositing the material in the middle of the plate. Gently raise lid and add about 15 c.c. of melted agar to each dish. Mix contents of each dish by gently rotating. Let agar solidify, invert and incubate 48 hours. Select a plate showing well-distributed, easily counted colonies and count the colonies present. Multiply the number of colonies counted by the times the milk in that plate was diluted. The result is the number of bacteria in 1 c.c. of the milk used. Why was a new pipette used for making each dilution of the milk? Why can transfers from the tubes to Petri dishes be made with a single pipette by beginning with the highest dilution and proceeding to the lowest?

9. The instructor should demonstrate how anaerobic cultures are made.
10. The instructor should demonstrate the technic of animal inoculation. What organisms are suspected and the results that will be obtained if they are present should be explained.
11. Preserved organs from autopsies of guinea pigs inoculated with *Myc. tuberculosis* and *Past. tularensis* should be shown and compared with normal organs.
12. If possible, an autopsy of a guinea pig infected with *Myc. tuberculosis* or *Past. tularensis* should be done.

EXERCISE 8. DESTRUCTION OF BACTERIA BY MECHANICAL AND PHYSICAL MEANS

Reference: Chapter XI

1. *Inspection of Sterilizing Equipment of the Hospital.*—Students accompanied by their instructor should make a tour of inspection of the sterilizing and disinfecting equipment of the hospital. In the operating room the methods of sterilizing surgical dressings and supplies should be demonstrated. In the clinical laboratory students should be shown autoclaves, dry air sterilizers, and Arnold sterilizers. Sterilization by filtration should be demonstrated. The tour should include a demonstration of the methods used in disinfecting clothing and the disposal of the waste materials from the hospital.
2. *Effects of Heat on Bacteria.*—Prepare five suspensions of *B. subtilis* and of *Bact. coli* by placing in sterile cotton-plugged test tubes 1 or 2 c.c. amounts of a suspension furnished by the instructor. Treat one tube of each suspension as indicated below:
 - a. Autoclave at 15 pounds' pressure for 15 minutes.
 - b. Stand in a pan of boiling water for 30 minutes.
 - c. Expose to free-flowing steam in an Arnold sterilizer for one hour.
 - d. Stand in a pan of water at 60° C. for one hour.
 - e. Use the fifth pair as a control.

Transfer a loopful of the suspension from each tube to a tube of broth and incubate at 37.5° C. for 24 hours. Record growth obtained in the following outline:

EXPOSURE TO HEAT	GROWTH OBTAINED	
	B. SUBTILIS	BACT. COLI
Autoclave; 15 lbs., 15 min.		
Boiling water; 30 min.		
Free-flowing steam; 1 hour		
60° C.; 1 hour		
Control		

Which tubes of the heated suspensions of *B. subtilis* show a growth? What does this indicate? What is the difference in the growth of *B. subtilis* and *Bact. coli*? What does this indicate? What part does spore formation play in this experiment?

3. The instructor will furnish you three swabs that have been dipped in a suspension of *B. subtilis* and three other swabs that have been dipped in a suspension of *Bact. coli*. Hold a swab from each suspension in a separate beaker of boiling water for one minute and then dip in a tube of nutrient broth. With the other swabs repeat the procedure using periods of five and ten minutes. Incubate the six tubes of broth 24 to 48 hours. Indicate growth obtained in the following table:

ORGANISM	PERIOD OF BOILING		
	ONE MINUTE	FIVE MINUTES	TEN MINUTES
<i>B. subtilis</i>			
<i>Bact. coli</i>			

What do the above findings indicate?

EXERCISE 9. DESTRUCTION OF BACTERIA BY CHEMICALS

Reference: Chapter XII

1. *Effect of Chemicals on Bacteria*.—The instructor will furnish you four sterile cotton-plugged tubes. The first contains 5 c.c. of 1:1,000 bichloride solution; the second, 5 c.c. of 5 per cent carbolic acid; the third 5 c.c. of some widely advertised antiseptic; and the fourth tube contains a broth suspension of staphylococci.

Proceed as follows: (a) to each tube of disinfectant add 0.5 c.c. of the broth suspension. Do not let run down side of tube. Mix by gently tapping the bottom of the tube. Place in water bath at 20° C. At the end of 5, 10 and 15 minutes transfer a loopful from each tube (except the tube containing the broth suspension) to a

tube of sterile broth. Label, giving organism and time held in water bath, incubate 48 hours and record growth on chart below using the plus sign to indicate growth and the minus sign to indicate absence of growth.

2. Repeat the above experiment using *B. subtilis* or other spore-forming organism instead of staphylococci. Record in chart.

DISINFECTANT	STAPHYLOCOCCUS			SPORE FORMER		
	5 MIN.	10 MIN.	15 MIN.	5 MIN.	10 MIN.	15 MIN.
Bichloride (1:1000)						
Phenol (5 per cent)						
Commercial disinfectant						

EXERCISE 10. IMMUNITY

Reference: Chapter XVI

1. Demonstration of the Phenomenon of Agglutination.—

(1) Set up a row of eight serological tubes.

(2) To the first tube add 1.8 c.c. physiological salt solution and to the remaining tubes add 1 c.c. physiological salt solution.

(3) To the first tube add 0.2 c.c. agglutinating serum against *Bact. typhosum* and mix.

(4) From tube 1 remove 1 c.c. and transfer to tube 2 and mix. From tube 2 remove 1 c.c.; transfer to tube 3 and mix. Continue transferring and mixing until tube 6 has been mixed. Discard 1 c.c. Tube 7 acts as a control.

(5) To all tubes add 1 c.c. of a suspension of killed typhoid bacilli. Calculate the dilution of agglutinating serum in each tube.

(6) Incubate at 37.5° C. for two hours.

(7) Note clumping of bacteria (agglutination) in the tubes containing the lower dilutions of agglutinating serum.

(8) Relative to this experiment fill out the following table:

TUBE	1	2	3	4	5	6	7
Dilution of Serum							
Agglutination*		.					

*Complete, partial or none.

Suppose the blood serum of a person instead of an artificial agglutinating serum had been used in this test and the results had been as indicated in above table. What would be the significance of the test? What would agglutination in tube 7 indicate? What is the name of the agglutination test from typhoid fever?

2. The instructor should demonstrate the microscopic agglutination test using living typhoid bacilli.
3. Stained smears of pus showing phagocytosis should be examined and compared with smears of pus in which phagocytosis is absent.

4. **Demonstration of the Phenomenon of Hemolysis.**—(1) Prepare a 1:100 dilution of antisheep hemolysin (having a titer of about 1:3,000) by adding 0.1 c.c. of hemolysin to 9.9 c.c. of physiological salt solution and mixing.

(2) Set up a row of ten clean serological tubes.

(3) To the first tube add 1 c.c. of the 1:100 hemolysin.

(4) To the remaining tubes, except the 9th, add 0.5 c.c. physiological salt solution.

(5) Remove 0.5 c.c. from the first tube; add to the second tube and mix. From the second tube remove 0.5 c.c., transfer to the third and mix. Continue in this manner until the contents of tube 7 have been mixed. Discard 0.5 c.c. of contents of this tube. Calculate the dilution of hemolysin in each tube.

(6) To the 9th tube add 0.5 c.c. of 1:100 hemolysin; to both the 9th and 10th tubes add 0.3 c.c. salt solution.

(7) To the first eight tubes add 0.3 c.c. of a 1:30 dilution of fresh guinea pig serum (complement).

(8) To all tubes add 1.7 c.c. of physiological salt solution. This is best done by adding 1.5 c.c. with a 10 c.c. pipette and then 0.2 c.c. with a 1 c.c. pipette.

(9) To all tubes add 0.5 c.c. of a 2 per cent suspension of sheep red blood cells. Incubate in water bath at 37.5° C. for one hour. Note solution of cells (hemolysis).

(10) Answer the following questions relating to this experiment:

a. What is the highest dilution of hemolysin showing complete hemolysis? -----

b. In what dilutions is hemolysis partial?-----

c. In what dilution does hemolysis cease?-----

d. Is hemolysis present or absent in the eighth tube? Why?--

e. Is it present in the ninth tube? Why?-----

f. What would hemolysis in the tenth tube indicate?-----

5. A group of recently completed Wassermann tests should be demonstrated. The principles of complement fixation should be discussed. What takes place in positive and negative tests should be explained.

EXERCISE 11. HYPERSENSITIVENESS

Reference: Chapter XVIII

1. **Demonstration of Anaphylaxis.**—Two or three weeks before this test prepare 3 guinea pigs by giving each an intraperitoneal injection of 0.25 c.c. of horse serum in 2 c.c. of sterile salt solution. At the present exercise inject each intravenously with 0.5 c.c. horse serum. Note results. Give complete description.
2. The instructor should demonstrate skin tests for hypersensitiveness.
3. The instructor should demonstrate the ophthalmic test for hypersensitiveness to horse serum.

EXERCISE 12. HOW INFECTION IS SPREAD**Reference: Chapter XIX**

1. **Bacteria on the Hands.**—Wash your hands in a sterile dish containing 300 c.c. of sterile water. Do not use soap. With a sterile pipette place 1 c.c. of the water in a sterile Petri dish. Melt a tube of agar and allow to cool to about 42° C. This point can be roughly determined by allowing the tube to cool until it feels just comfortable to the back of the hand. Pour the cooled medium into the dish and mix the water with it by rotating the dish. Let medium harden, invert dish and incubate at 37.5° C. for 24 to 48 hours. Note number of colonies and different kinds of colonies.
2. **Bacteria in the Breath.**—You will be furnished three agar plates. Remove lid of one, hold plate about six inches from your mouth and breathe normally but directly upon medium. The second plate is held in the same manner but about a foot from the mouth while you cough violently. The third is held at arm's length from the mouth while coughing. After the lids have been replaced, invert plates and incubate 24 to 48 hours. Which plate has the most colonies? Why?
3. Each student should make cultures from different portions of the body as the nose, throat, ears, etc., using tubes of media that would be likely to grow any organism present. Incubate at 37.5° C. for 24 to 48 hours. Make smears from cultures and stain by Gram's method. Note shape of bacteria and whether gram-positive or gram-negative.
4. **Bacteria on Insects.**—Prepare a Petri dish of agar. When the agar has hardened, allow an insect such as a fly to crawl for a time on the surface of the agar under the cover. Invert the plate and incubate 24 to 48 hours. Note colonies.
5. **Bacteria on Finger Tips.**—Gently touch the ends of your fingers to the surface of an agar plate. Incubate plate for 24 hours and examine.

EXERCISE 13. BACTERIOLOGY OF WATER**Reference: Chapter XX**

- 1. Plate Count of Bacteria in Water.**—The instructor will furnish you (1) a sample of water, (2) sterile pipettes, (3) three tubes, each of which contains 9 c.c. of sterile water, (4) three sterile Petri dishes and (5) three tubes of agar. Proceed as follows:

(1) To one tube of sterile water add 1 c.c. of the sample and mix.

(2) With a new pipette transfer 1 c.c. from this tube to the second tube and mix.

(3) Repeat the procedure by taking a new pipette, transferring 1 c.c. from the second to the third tube and mixing. Calculate the dilution of water in each tube. Why is a new pipette used for each procedure?

(4) With a new pipette transfer 1 c.c. from each tube to a Petri dish beginning with the highest dilution and proceeding to the lowest. Why do you go from the highest to the lowest dilution?

(5) Melt tubes of agar in water bath, let cool to 42° to 45° C. and add one tube to each Petri dish.

(6) Mix with water by rotating, let agar solidify, invert plates and incubate at 37.5° C. for 48 hours.

(7) Select a plate on which the colonies are distinctly separated and count the colonies. From the dilution calculate the bacterial content of the water per c.c.

- 2. Presumptive Test for Bact. coli in Water.**—The instructor will furnish you a sample of contaminated water, sterile pipettes and nine fermentation tubes containing lactose broth. Proceed as follows:

(1) To each of two tubes add 0.1 c.c. of the sample.

(2) To two more tubes add 1 c.c. of the sample.

(3) To the remaining five tubes add 10 c.c. portions of the sample.

(4) Mix water with contents of tube by gently rolling tube between the palms. Do not let the contents of the tube come in contact with the plug.

(5) Place in incubator at 37.5° C. and examine at end of 24 and 48 hours. For each period note the percentage

of gas formed in each tube as indicated by the portion of the collecting tube that is filled with gas.

3. The instructor should demonstrate plates made from tubes in which gas formation has occurred. The characteristics that differentiate colonies of *Bact. coli* from other organisms on the medium used should be explained.
4. The methods of differentiating fecal from nonfecal *Bact. coli* should be demonstrated.

EXERCISE 14. BACTERIOLOGY OF MILK

Reference: Chapter XXI

1. **Plate Count of Bacteria in Milk.**—The method to be used here is the same as in experiment 1, Exercise 13, except that milk is used instead of water and the dilution bottles contain 99 c.c. instead of 9 c.c. of sterile water. After the milk has been plated and incubated for 48 hours, count the colonies and calculate the number of bacteria per c.c. of the original milk. Are the colonies on the plates all alike or are there several varieties?
2. **Effect of Pasteurization on Milk.**—The instructor will furnish you two tubes of raw milk, two 99 c.c. dilution bottles, two tubes of nutrient agar and the necessary pipettes. Proceed as follows: (1) place one tube of milk in a water bath and raise the temperature of the water to 65° C.; hold at this temperature for 30 minutes; (2) make a 1:100 dilution of this milk and the unheated milk. Plate 1 c.c. of each dilution and incubate at 37.5° C. for 48 hours. Which plate contains more bacteria? Why? What is the bacteria count on each plate? How much is this per c.c. of milk?

EXERCISE 15. THE COLON-TYPHOID GROUP OF BACTERIA

Reference: Chapter XXII

1. Students should be shown smears, hanging-drop preparations and cultures of *Bact. typhosum*, *Bact. coli*, and *Bact. dysenteriae*.

2. The instructor should review the agglutination test and discuss the significance of the Widal test for typhoid fever. The presence of "H" and "O" agglutinins should be demonstrated and their significance should be discussed.
3. Various cultures of *Bact. typhosum* and other fecal organisms on media designed to differentiate these organisms should be examined. Suggested media are: Endo's medium, eosin-methylene blue, Russell's double sugar, bismuth-sulphite and lead acetate agars.

EXERCISE 16. THE ACID-FAST BACTERIA

Reference: Chapter XXIII

1. Using a specimen of sputum that has been autoclaved, prepare smears and make acid-fast stains. Make a drawing in colors (red and blue).
2. The instructor should make an autopsy on a tuberculous guinea pig. The effect of the bacilli on different organs should be demonstrated and discussed.
3. Various tuberculous organs of human origin should be shown. Microscopic sections of tubercles should be examined.
4. The method of inoculating a guinea pig to detect the presence of *Myco. tuberculosis* should be demonstrated.
5. The technic of the tuberculin test and a positive result should be demonstrated by the instructor.
6. Cultures of *Myco. tuberculosis* should be demonstrated.
7. The students should examine smears of *Myco. leprae* furnished by the instructor.

EXERCISE 17. BACTERIA PRODUCING EXTRACELLULAR TOXINS

Reference: Chapter XXIV

1. Students should examine smears showing diphtheria and tetanus bacilli. Cultures of *C. diphtheriae* should be observed.

2. Smears showing the difference in *C. diphtheriae* and diphtheroid bacilli should be examined. The value of differential stains should be discussed.
3. The exact technic of taking a throat culture should be demonstrated. The precautions to be observed should be stressed.
4. A positive and negative virulence test should be demonstrated.
5. A positive Schick test should be demonstrated.

EXERCISE 18. THE PYOGENIC COCCI

Reference: Chapters XXV and XXVI

1. Prepare smears from a specimen of sputum containing pneumococci. Stain by Gram's method. Make drawing. Note capsule formation.
2. Make smears from a culture of pneumococci. Stain by Gram's method. What important structure is not as well developed in cultured pneumococci as in those from the body?
3. The instructor should discuss the methods of typing pneumococci.
4. Examine cultures and make Gram stains of streptococci. Make drawing.
5. Blood agar plates showing pneumococci and different types of streptococci should be examined. The differential characteristics of these organisms when grown on blood agar should be explained by the instructor.
6. A positive Dick test should be demonstrated.
7. Cultures of staphylococci should be examined. Make smears and stain by Gram's method. Note pigment produced by growth of staphylococci on medium.
8. Students should examine smears of pus containing gonococci (stained with methylene blue and by Gram's method). Smears of purulent cerebrospinal fluid stained in the same manner should be examined. Note the similarity of the two organisms.
9. The instructor should demonstrate the method of taking cultures to detect meningococcus carriers.

EXERCISE 19. SPIROCHETES**Reference: Chapter XXXII**

The instructor should demonstrate stained smears of various spirochetes.

EXERCISE 20. FUNGI**Reference: Chapter XXXIII**

1. Examine a natural growth or a culture of mold with the naked eye and with a strong hand lens. Note color and general appearance.
2. Mount some of the growth in a drop of water and examine with the microscope. Are the hyphae septate or non-septate? Note presence of nuclei. Making a drawing.
3. Rub up a small portion of yeast cake in water. Place a drop on slide, cover with a cover glass and examine.

EXERCISE 21. PROTOZOA**Reference: Chapter XXXIV**

1. Procure a few drops of hay infusion containing *Paramecia*; place on a clean slide and add a few grains of sand to hold cover glass away from the organisms. Gently apply cover glass. Note movement of *Paramecia*. Do they seem to have a purposeful or aimless movement? Make a sketch of a quiescent organism.
2. *Digestion by Paramecia*: Place a suspension of India ink on a slide and add a drop of material containing *Paramecia*. Note currents in oral groove. Note ingestion, attempt at digestion (India ink is indigestible) and expulsion.
3. Examine prepared slides showing malaria parasites, Trypanosomes, etc.
4. Mix a small portion of the contents of a guinea pig's caecum with a drop of salt solution on a slide. Superimpose a cover glass and examine with low power and high dry objective. Look especially for the large ciliate (*Balantidium*) that often inhabits the caecum and for various flagellates that may be found. Note comparative size of protozoa and bacteria. Make a drawing of each type of protozoon found.

II. EXERCISES IN PATHOLOGY

EXERCISE 22. DEGENERATIONS, INFILTRATIONS, PIGMENTATIONS, AND CONCRETIONS

Reference: Chapter XL

1. Students should examine sections of skin from white and Negro persons. What difference is noted?
2. The instructor should demonstrate organs showing cloudy swelling, fatty degeneration, necrosis, and calcification.
3. The instructor should demonstrate and explain the formation of various concretions.

EXERCISE 23. NECROSIS, GANGRENE, AND SOMATIC DEATH

Reference: Chapter XLI

The instructor should demonstrate specimens showing moist and dry gangrene. The important differential characteristics should be noted.

EXERCISE 24. DISTURBANCES OF CIRCULATION

Reference: Chapter XLII

1. Microscopic sections of normal tissues and the same kind of tissues showing passive congestion should be examined and compared.
2. The instructor should demonstrate thrombosed vessels.
3. Specimens of clotted blood and blood to which an anti-coagulant has been added should be centrifuged. The ratio of cells to liquid should be noted. In which tube is the liquid plasma? In which is the liquid serum?

EXERCISE 25. INFLAMMATION AND REPAIR

Reference: Chapter XLIII

1. Students should examine microscopic sections of normal and inflamed tissues.
2. Microscopic sections of normal appendices should be compared with those showing different types of appendicitis.
3. Smears of pus from acute and chronic inflammatory processes should be examined. What type of cell predominates in each smear? The relation of normal white blood cells and pus cells should be explained.

4. Gross specimens showing abscesses, sinuses, and ulcers should be demonstrated by the instructor.

EXERCISE 26. INFECTIOUS DISEASES

Reference: Chapter XLIV

1. A lung showing lobar pneumonia should be demonstrated and compared with a normal lung.
2. The intestinal lesions of typhoid fever should be demonstrated.
3. Various specimens showing tuberculosis should be demonstrated.
4. Gummas and other lesions of syphilis should be demonstrated.

EXERCISE 27. DISTURBANCES IN THE SIZE, GROWTH, AND DEVELOPMENT OF CELLS

Reference: Chapter XLVI

The instructor should demonstrate specimens showing atrophy and hypertrophy.

EXERCISE 28. TUMORS

Reference: Chapter XLVII

Various tumors, malignant and nonmalignant, should be demonstrated. Primary and secondary growths of malignant tumors should be examined and discussed. The difference between benign and malignant tumors should be fully explained.

EXERCISE 29. DISEASES OF THE HEART AND BLOOD VESSELS

Reference: Chapter XLIX

1. Hypertrophied and dilated hearts should be demonstrated.
2. Specimens of various valvular diseases of the heart should be demonstrated.
3. An aneurysm should be demonstrated and compared with the same vessel in its normal state.
4. Varicose veins should be demonstrated.

EXERCISE 30. DISEASES OF THE BLOOD**Reference: Chapter L**

1. The method of estimating hemoglobin should be demonstrated. Students should estimate the hemoglobin of each other.
2. The method of counting blood cells should be demonstrated and explained.
3. Smears of normal blood and blood from patients with leucemia and profound anemia should be examined.

EXERCISE 31. DISEASES OF THE LYMPHATIC SYSTEM**Reference: Chapter LI**

The instructor should exhibit specimens showing various diseases of the lymph nodes and spleen.

EXERCISE 32. DISEASES OF THE RESPIRATORY SYSTEM**Reference: Chapter LII**

The instructor should demonstrate specimens showing bronchiectasis and emphysema.

EXERCISE 33. DISEASES OF THE NERVOUS SYSTEM**Reference: Chapter LIII**

1. Specimens of normal and purulent cerebrospinal fluid should be demonstrated.
2. Specimens of hydrocephalus, brain abscesses, and brain tumors should be demonstrated.

EXERCISE 34. DISEASES OF THE DIGESTIVE SYSTEM**Reference: Chapter LIV**

1. The instructor should demonstrate specimens of gastric ulcer and gastric cancer.
2. The method of determining the amount of the various components of the stomach contents should be demonstrated.
3. An intestinal diverticulum should be demonstrated.

4. Specimens showing intestinal obstruction, intussusception, and volvulus should be demonstrated.
5. Various intestinal worms should be demonstrated and their eggs should be examined.
6. Specimens showing the different types of appendicitis should be demonstrated.
7. The students should be shown various types of gallstones.

EXERCISE 35. DISEASES OF THE URINARY SYSTEM

Reference: Chapter LV

1. Kidneys showing various forms of nephritis should be demonstrated and compared with a normal kidney.
2. Specimens showing tuberculosis of the kidney should be demonstrated.
3. Renal tumors should be demonstrated.
4. Renal and vesical calculi should be demonstrated.
5. The students should be allowed to make simple chemical examinations for pathological constituents of urine.
6. The instructor should demonstrate and the students should examine abnormal microscopic elements of urine.

EXERCISE 36. DISEASES OF THE FEMALE ORGANS OF REPRODUCTION

Reference: Chapter LVI

1. Specimens showing ovarian cysts and tumors should be demonstrated.
2. Specimens of pyosalpinx and hydrosalpinx should be demonstrated.
3. Specimens of uterine fibroids, cancer of the cervix, and cancer of the body of the uterus should be demonstrated.
4. Various inflammatory conditions, tumors, and cystic conditions of the breast should be demonstrated.

EXERCISE 37. DISEASES OF THE BONES AND JOINTS

Reference: Chapter LIX

1. Various inflammatory conditions, tuberculous and syphilitic processes of the bones and joints, should be demonstrated.
2. Various tumors of the bones should be demonstrated.

PART IV

GLOSSARY

- Abscess**, a circumscribed collection of pus.
- Accelerate**, to increase in rapidity.
- Accelerated reaction**, a reaction following the vaccination of a person partially immune to smallpox.
- Acetone bodies**, a term used to denote acetone, diacetic acid, and oxybutyric acid collectively.
- Achlorhydria**, absence of hydrochloric acid in the gastric juice.
- Acid-fast**, bacteria that do not lose their stain when treated with an acid after being stained with an aniline dye (Ex.—*Myco. tuberculosis*).
- Acidosis**, a condition characterized by a decrease in the alkalinity of the blood.
- Acquired immunity**, an immunity that a person acquires after birth.
- Active carrier**, one who becomes a carrier after recovery from a disease.
- Active immunity**, an immunity brought about by the activity of the body cells of the one becoming immune.
- Acuminate**, pointed or tapering.
- Acute disease**, a disease that runs a rapid course and has more or less severe symptoms.
- Adenopathy**, disease of the lymph nodes.
- Adhesion**, the adherence or knitting together of two surfaces.
- Aerate**, to charge with air or other gas.
- Aerobe**, an organism whose growth requires the presence of oxygen.
- Aerosols**, finely divided antiseptic solutions sprayed into the air.
- Afferent**, bringing to or into.
- Agar**, a gelatinous substance, prepared from seaweed, used as a base for solid culture media.
- Agglutinins**, antibodies that cause agglutination.
- Agglutininogen**, any substance which, acting as an antigen, stimulates the production of agglutinins.
- Albinism**, congenital absence of pigment from the skin and other structures.
- Albolene**, an oil derived from Russian mineral oil.
- Albuminuria**, the presence of albumin in the urine.
- Algid**, cold. An algid fever is one in which the patient goes into a state of collapse.
- Alimentary tract**, the digestive tract.
- Alkaloid**, a basic substance found in plants which is usually the part of the plant that has medicinal properties.
- Allergen**, a substance that is capable of bringing about an allergic state when introduced into the body.

Allergic, caused by allergy.

Allergy, a hypersensitive state in which the affected person exhibits unusual symptoms upon coming in contact with an allergen.

Alveolar process, the portion of the jaw in which the teeth are embedded.

Alveolus, a cavity or sac.

Amboceptor, a substance that enters into combination with cells and complement to produce dissolution of the cells.

Ambulatory, not confined to bed.

Ameba, *amoeba*; pl. *amebas*, *amoebae*, a protozoon that moves by extruding fingerlike processes (pseudopods).

Amebiasis, infection with pathogenic amebas. Acute amebiasis is known as amebic dysentery.

Ameboid, *amoeboid*, resembling an ameba.

Amitosis, direct cell division.

Ampulla, a saccular dilatation of a canal.

Anaerobe, an organism that grows only or best in the absence of oxygen.

Anaphylaxis, a state of hypersusceptibility to a protein resulting from a previous introduction of the protein into the body.

Anasarca, edema of the subcutaneous tissues.

Anemia, an impoverished condition of the blood due to a reduction in red blood cells, hemoglobin, or both.

Aneurysm, a dilatation of an artery due to weakness of its wall.

Angioma, a tumor composed of blood or lymph vessels.

Animate, having life.

Ankylosis, stiffening or fixation of a joint.

Anoxemia, lack of oxygen in the blood.

Antagonism, mutual resistance.

Antibacterial serum, an antiserum that destroys or prevents the growth of bacteria.

Antibiotic, an agent produced by one organism which will destroy another organism.

Antibody, an agent in the body, especially in the blood, that destroys or renders inactive certain foreign substances that gain access to the body, particularly bacteria and their products.

Anticoagulant, an agent that prevents coagulation.

Antigen, a substance which when introduced into the body causes the body to produce antibodies.

Antiluetic, *antisypilitic*. A drug used in the treatment of syphilis.

Antiseptic, a substance which prevents the growth of bacteria.

Antiserum, an immune serum.

Antitoxin, an immune serum which neutralizes or prevents the action of a toxin.

Anuria, complete suppression of urine.

- Apoplexy**, a sudden loss of consciousness followed by paralysis due to cerebral hemorrhage, thrombosis, or embolism.
- Appendical**, relating to the appendix.
- Apposition**, side by side.
- Aphthous**, characterized by the presence of small ulcers.
- Aquatic**, pertaining to water. Living in water.
- Arachnoid mater**, the middle of the three membranes covering the brain and spinal cord.
- Argyll Robertson pupil**, a pupil that reacts to distance but not to light.
- Arteriole**, a small artery that ends in a capillary.
- Arthritis**, inflammation of a joint.
- Ascites**, an abnormal collection of fluid in the abdominal cavity.
- Ascitic fluid**, fluid from the abdominal cavity of a person with ascites.
- Aseptic**, free from septic bacteria.
- Asphyxia**, a condition in which the heart continues to beat after respiration has stopped.
- Aspirate**, to draw by suction as when fluid is removed with a syringe or material is drawn into the lungs during inspiration.
- Ataxic gait**, a gait characterized by lack of muscular coordination.
- Atony**, lack of tone or tension. Flaccidity.
- Atresia**, congenital absence or an abnormal closure of a normal opening or passage.
- Atrium**; pl. *atria*, the upper chamber of each half of the heart. **Auricle**.
- Autoclave**, an apparatus for sterilizing by steam under pressure.
- Autogenous vaccine**, a vaccine made from a culture of bacteria obtained from the patient himself.
- Autoinfection**, an infection of one part of the body by bacteria derived from some other part of the body.
- Autopsy**, an examination of the internal organs of the dead body.
- Autotrophic**, organisms that are capable of forming their proteins and carbohydrates out of inorganic salts and carbon dioxide.
- Bacillus**; pl. *bacilli*, a rod-shaped bacterium.
- Bacteremia**, a condition in which bacteria are in the blood stream but do not multiply there.
- Bacteria**; sing. *bacterium*, vegetable unicellular organisms. **Germs**.
- Bacteriology**, the science that treats of bacteria.
- Bacteriolysins**, antibodies which cause the solution of bacteria in the presence of complement.
- Bacteriophage**, a substance which develops in a culture and dissolves the bacteria in the culture.
- Bang's disease**, contagious abortion of cattle.
- Benign**, mild in character. As applied to tumors, not malignant; i. e., does not spread to different parts of the body and does not recur after removal.
- Bilateral**, having two sides or occurring on both sides.

Biological, relating to biology.

Biological transfer of infection, a mode of transfer of infection from host to host by an animal or insect in which the agent causing the disease undergoes a cycle of development in the animal or insect.

Biology, that science which treats of living things, both animals and plants.

Biotherapy, the treatment of disease with a living agent or its products.

Blastomycosis, infection with blastomyces.

Blood serum, the fluid that exudes when blood clots. It is blood plasma without fibrinogen.

Boil, an abscess of the skin and subcutaneous tissue.

Bossing, the formation of knoblike protuberances.

Botany, that science which treats of plant life.

Brownian motion, a peculiar dancing motion possessed by finely divided particles in suspension. Frequently seen when examining liquid suspensions of bacteria.

Cachexia, a general wasting away of the body due to lack of nutrition.

Caecum, (see cecum).

Calcium-bilirubin, a combination of calcium and bile pigment.

Callus, a hard bony substance thrown out at the site of a fracture. The callus takes part in the healing of the fracture and then gradually disappears.

Calyces; sing. *calyx*, the recesses in the pelvis of the kidney into which the opening of the pyramids project.

Cancellous bone, the inner spongy portion of bone.

Capsule, an envelope that surrounds certain bacteria. A membranous structure surrounding a joint or tumor.

Carbohydrates, a class of compounds that are composed of carbon, hydrogen, and oxygen, the latter two in the proportion to form water. To this class belong the sugars, starches, and cellulose.

Caries, decay of bone characterized by thinning, increased friability, and pus formation.

Carrier, a person in apparent health who harbors a pathogenic agent in his body.

Caryosome, a chromatin mass on the linin network of the cell nucleus. Caryosomes form the chromosomes during cell division.

Cast, a mold of a tubular structure, particularly of the kidney tubules.

Catabolism, the breaking down of complex bodies into waste products of more simple composition.

Cataract, an opacity of the crystalline lens or its capsule.

Catarrhal, characterized by an outpouring of mucus.

Cecum, the pouchlike structure that forms the first part of the large intestine. The appendix arises from the cecum.

- Cell**, a minute structure which forms the anatomical and physiological basis of all animals and plants; i. e., all animals and plants are made up of one or more cells, and their activities depend on the combined activities of the cells that compose them.
- Cellulitis**, inflammation of the cellular or connective tissue.
- Centrifugalization**, the process of subjecting to centrifugal force.
- Centrifugalize**, to subject to centrifugal force.
- Centrosome**, a small deeply staining body seen in the cytoplasm of certain cells. It plays an important part in cell division.
- Cervical**, pertaining to the neck.
- Cervix uteri**, the lower cylindrical portion of the uterus.
- Chancre**, the initial lesion of syphilis.
- Charcot-Leyden crystals**, crystals found in the sputum in bronchial asthma.
- Chemotaxis**, reaction to a chemical whereby cells are attracted (positive chemotaxis) or repelled (negative chemotaxis) by the chemical.
- Chemotherapeutic agent**, an agent used in chemotherapy.
- Chemotherapy**, the treatment of disease by the administration of drugs which destroy the causative organism of the disease but do not injure the patient.
- Cheyne-Stokes respiration**, a type of respiration in which the respiratory movements increase in depth to a certain point and then decrease after which all respiratory movements cease for thirty to sixty seconds and then begin again as before.
- Chilblains**, a burning, itching erythema of the hands, feet, nose, and other parts of the body caused by repeated exposure to damp cold.
- Chlorophyll**, the coloring matter of green plants.
- Choked disk**, inflammation and serous infiltration of the optic nerve at the point where it enters the retina.
- Cholangitis**, inflammation of the bile ducts.
- Cholecystitis**, inflammation of the gallbladder.
- Cholesterol**, an alcohol ($C_{27}H_{46}OH$) occurring in the form of scales with a notched corner, that is found in blood, bile, egg yolk, seeds of plants, and elsewhere.
- Chorea**, a disorder that usually occurs in childhood and is characterized by involuntary spasmodic movements of the limbs and facial muscles. St. Vitus' dance.
- Chorionic villi**, vascular processes which occur on the outer layer of the fetal membranes during the early stages of development and later enter into the formation of the placenta.
- Chromatin granules**, caryosomes.
- Chromidia**, chromatin material scattered throughout the protoplasm of cells, without organized nuclei.

- Chromosomes**, rod-shaped masses of chromatin that appear in the cell nucleus during mitosis. They play an important part in cell division and transmit the hereditary characteristics of the cell.
- Chyme**, the partially digested food that passes from the stomach to the duodenum.
- Cicatricial**, relating to a cicatrix.
- Cicatrix**, a scar.
- Cilia**; sing. *cilium*, hairlike processes that spring from certain cells and by their action create currents in liquids. If the cells are fixed, the liquid is caused to move, but if the cells are those of unicellular organisms suspended in the liquid, the cells move.
- Ciliates**, unicellular organisms that move by means of cilia.
- Circumscribed**, confined to a limited space.
- Cirrhosis**, degeneration of the active tissue of an organ, with an increase in the supporting connective tissue.
- Coagulase**, an enzyme that causes coagulation.
- Coccus**; pl. *cocci*, a spherical-shaped bacterium.
- Collateral circulation**, the circulation which is maintained by way of small anastomosing vessels when a main vessel is obstructed.
- Colony**, a visible growth of bacteria on a culture medium; all the progeny of a single preexisting bacterium.
- Color index**, the amount of hemoglobin in a red blood cell as compared with the normal.
- Coloration**, state of being colored.
- Comatose**, in a state of profound unconsciousness from which the patient cannot be aroused.
- Communicable**, capable of being communicated.
- Compensation**, as applied to disease of the heart, the maintenance of the circulation in cases of valvular defects of the heart by hypertrophy of the heart muscle; more generally, the supplying of a deficiency or making one part do the work of another.
- Complement**, a substance found in normal blood which is capable of destroying bacteria or other cells when brought in contact with them by means of amboceptor.
- Complement fixation**, the destruction or inactivation of complement brought about by the combination of antigen, antibody, and complement. This is the basis of the complement fixation tests for syphilis and certain other diseases.
- Concentric**, having a common center.
- Conception**, the act of becoming pregnant.
- Concomitant**, occurring at the same time.
- Concretion**, a solid or hardened mass of foreign material or normal material that has become inspissated.
- Condyloma**, a wartlike growth.

Congenital, existing at the time of birth.

Congestion, hyperemia.

Constitutional, relating to the make-up of the body as a whole.

Contagious, highly communicable. In common parlance, a disease that is easily "caught."

Contamination, soiling with infectious material.

Continuity, uninterrupted connection or succession.

Convalescent carrier, a carrier who harbors the organisms of a disease during convalescence from the disease.

Convalescent serum, the blood serum of a person recently recovered from a disease. In a few cases the injection of convalescent serum seems to be of value in treatment or in preventing the occurrence of the disease in others.

Conveyer, one who conveys.

Corpus luteum, a yellow body at the surface of the ovary brought about by changes following the rupture of a Graafian follicle.

Corrosive, having the power to corrode or eat away.

Counterstain, a second stain of a different color applied to a smear for purposes of rendering organisms stained with a primary stain more distinct.

Craniotabes, a condition characterized by areas of thinning and softening of the bones of the skull.

Crisis, a sudden change in the course of a disease. Diseases which terminate by a sudden change for the better are said to end by crisis.

Crypt, a simple gland or minute culdesac. A collection of lymphoid tissue.

Culture, a growth of microorganisms on a culture medium. To grow microorganisms on a culture medium.

Culture media; sing. *medium*, artificial food material upon which bacteria are cultivated.

Cutaneous, pertaining to the skin. Cutaneous inoculation is carried out by rubbing the infectious material on the abraded skin.

Cyanosis, a blue or purple color of the skin due to lack of oxygen in the blood.

Cyst, an abnormal saccular structure containing liquid, air, or solid material. A stage in the life history of certain protozoa during which time the organism is protected by a surrounding wall.

Cystitis, inflammation of the bladder.

Cytolysin, an antibody that is capable of causing cells to dissolve.

Cytoplasm, the protoplasm of a cell other than that of the nucleus.

Dakin's solution, a neutral solution of sodium hypochlorite used in the disinfection of wounds.

Debilitating, weakening.

Decidual, pertaining to the decidua, the altered mucous membrane of the pregnant uterus which forms a covering for the fetus.

Decompensation, a failure of compensation in heart disease.

Defibrinated, having had its fibrin removed as in the case of blood that has been defibrinated to prevent clotting.

Deglutition, swallowing.

Dementia, insanity characterized by the loss of such mental faculties as reason, memory, etc.

Deodorant, a substance that destroys unpleasant odors.

Dependent, hanging down.

Desquamation, the shedding of the superficial layer of the skin in scales or shreds.

Devitalize, to deprive of life.

Diabetes insipidus, a disease characterized by the excretion of a large amount of urine that is of low specific gravity and does not contain sugar.

Diabetes mellitus, a primary fault of the islands of Langerhans of the pancreas characterized by a deficient production of insulin. The lack of insulin leads to faulty carbohydrate metabolism with an increase in the amount of glucose in the blood and its escape into the urine.

Diaphysis, the shaft of a long bone.

Diatomaceous earth, earth made up of the petrified bodies of diatoms. Diatoms are unicellular algae.

Dick test, a skin test to determine susceptibility to scarlet fever.

Differential blood count, the determination of the percentage of the different types of leucocytes in the blood.

Dilatation, enlargement of a cavity, canal, or opening.

Diplococci, cocci occurring in pairs.

Direct contact, spread of a disease more or less directly from person to person.

Disinfectant, a substance that disinfects.

Disinfection, the destruction of all disease-producing organisms and their products.

Dissociation, separation, dissolution of relations.

Diverticulum, a pouch or sac opening out from a tubular organ.

Droplet infection, infection conveyed by the spray thrown off from the mouth and nose while talking, coughing, etc.

Dropsy, an excessive accumulation of fluid in the tissues or cavities of the body.

Duct, a tubular structure giving exit to a fluid.

Dyscrasia, a morbid state.

Ecchymosis, a purple or blue area caused by extravasation of blood into the skin. They have the same origin as petechiae, but are larger.

Eclampsia, convulsions of toxic origin occurring during the latter part of pregnancy or during labor.

Ecto-enzyme, an enzyme that is excreted through the membrane of the cell forming it, into the surrounding medium.

Ectopic, out of place. **Ectopic pregnancy**, a pregnancy occurring outside the cavity of the uterus.

Ectoplasm, the outer clear zone of the cytoplasm of a unicellular organism.

Edema, an abnormal accumulation of fluid in the tissues.

Efficacy, power to produce effects.

Effusion, the escape of fluid from the blood vessels or lymphatics into the tissues or body cavities.

Ehrlich's side-chain theory, a theory of immunity advanced by Paul Ehrlich.

Embolism, obstruction of a vessel by an object floating in the blood stream.

Embolus, an object that causes an embolism. The most common emboli are portions of thrombi, portions of heart valves, agglutinated bacteria, tumor cells, air, fat, etc.

Embryonic layers, (see germ layers).

Emphysema, dilatation of the pulmonary air sacs. The presence of air in the tissues of a part.

Emphysematous, relating to or affected with emphysema.

Empyema, a collection of pus in a cavity. When used without qualifications it is a collection of pus in the pleural cavity.

Encapsulated, surrounded by a capsule.

Endemic, more or less continuously present in a community.

Endocarditis, inflammation of the endocardium or lining membrane of the heart. It is usually confined to the endocardium of one or more valves.

Endocrine, a gland of internal secretion.

Endo-enzyme, an enzyme that is liberated only when the cell that produces it disintegrates.

Endogenous, originating within the organism.

Endometrial, pertaining to the endometrium.

Endometrioma, a tumor composed of endometrium.

Endometriosis, the occurrence of endometrium in locations other than the lining of the uterus.

Endometritis, inflammation of the endometrium.

Endometrium, the mucous membrane lining the uterus.

Endoplasm, a zone of granular cytoplasm found near the nucleus of many unicellular organisms.

Endostitis, inflammation of the medullary cavity of a bone.

Endotoxin, a toxin that is liberated only when the cell producing it disintegrates.

Enzyme, a substance secreted by a living cell which is capable of bringing about changes in other substances without undergoing any change itself.

Eosinophile, a granular leucocyte whose granules stain with eosin.

Epicardium, the layer of the pericardium immediately enveloping the heart.

Epidemic, a disease that attacks a large number of people in a community at the same time.

Epidemiology, the science that treats of epidemics.

Epileptiform, resembling epilepsy.

Epiphyseal, relating to an epiphysis.

Epiphysis, a portion of a long bone developed from a center of ossification distinct from that of the shaft and separated from the shaft at first by a layer of cartilage. The ends of the long bones of the limbs are formed in this manner.

Epiphysitis, inflammation of an epiphysis.

Epitrochlear, relating to the epitrochlea or inner condyle of the humerus.

Erode, to wear away.

Exacerbation, an increase in severity of a disease.

Exanthematous, relating to an exanthema or general disease accompanied by a skin eruption.

Excision, the operative removal of a portion of the body.

Excrete, to cast out waste products.

Exfoliate, to come off in strips or sheets, particularly the stripping of the skin after certain exanthematous diseases.

Exogenous, coming from the outside of the body.

Exostosis, a bony outgrowth springing from the surface of a bone.

Exotoxin, a toxin that is secreted by a microorganism into the surrounding medium.

Extradural, on the outside of the dura mater.

Extragenital, unrelated to the genital tract.

Extraneous, outside the organism and not belonging to it.

Exudate, fluid or formed elements of the blood extravasated into the tissues or cavities of the body.

Facultative, having the power to do a thing although not ordinarily doing it. **Ex**—a facultative anaerobe is an organism that can live in the absence of oxygen but does not ordinarily do so.

Familial, affecting several members of the same family.

Ferment, an enzyme.

Fermentation, the breaking down of complex organic compounds, particularly carbohydrates by enzymes.

Fibroma, a nonmalignant tumor composed of connective tissue.

Fibrinolysin, a substance which dissolves a clot by destroying its fibrin.

Fibrosed, characterized by a marked increase in fibrous tissue.

Filtrate, a liquid that has passed through a filter.

Filtration, the process of passing a liquid through a filter.

Fimbria, a fringelike structure.

Fimbriated, having fimbriae. The fimbriated extremity of the fallopian tube is the fringed abdominal end of the tube.

Fissure, a crack or slit in a mucous membrane.

Fistula, an abnormal passage leading from a body cavity or hollow organ to the surface or to another body cavity or hollow organ.

Fix, to make firmly attached or set.

Flagella; sing. *flagellum*, a long hairlike process attached to the extremity of a microorganism having a lashing activity that causes the organism to move. One or more flagella may be attached to one or both ends of the organism.

Flagellates, organisms that move by means of flagella.

Flatulence, the presence of an excessive amount of gas in the stomach and intestines.

Focal infection, a localized site of more or less chronic infection from which bacteria or their products are spread to other parts of the body.

Foramen magnum, an oval opening in the occipital bone through which the lower portion of the medulla oblongata passes.

Foramen ovale, an opening in the septum between the atria of the fetal heart. This foramen closes at birth or soon thereafter.

Fractional sterilization, the heating of the material to be sterilized at a low temperature (60°-100°C.) for a given period, most often one hour, for three or four successive days and storing under conditions suitable for bacterial growth between sterilizations. The heating kills vegetative bacteria and the spores develop into vegetative bacteria during the periods between heatings.

Fumigation, exposure to the fumes of a gas that destroys bacteria, vermin, etc.

Fundus, the portion of a hollow organ farthest removed from the outlet.

Fungating, growing exuberantly, like a fungus.

Fungoid, resembling a fungus.

Fungus; pl. *fungi*, cellular vegetable organisms that feed on organic matter; molds, mushrooms, etc.

Furuncle, a boil.

Furunculosis, the presence of a number of furuncles or boils.

Fusiform, spindle-shaped.

Gamete, a cell, either male or female, that undergoes sexual reproduction.

Ganglion, an aggregation of nerve cells within the brain or along the course of a nerve. A cystic swelling connected with a tendon sheath.

Gastritis, inflammation of the stomach.

Gene, structures in the chromosomes that determine hereditary characteristics.

General infection, one that involves the whole body.

Genital, relating to the reproductive organs.

Germ, a microbe.

Germ cell, a cell specialized for reproduction.

Germicide, an agent that destroys germs.

Germ layers, the primary layers of cells formed early in the development of the embryo and from which the tissues and organs develop.

Gestation, pregnancy.

Globulin, a class of proteins characterized by being insoluble in water but soluble in weak solutions of various salts. Globulin is one of the important proteins of blood plasma.

Glucose, dextrose, grape sugar.

Glycosuria, the excretion of sugar (glucose) in the urine.

Graafian follicles, vesicular bodies in the ovary, each of which contains an ovum.

Gram-negative, bacteria that are decolorized when stained by Gram's method, i.e., they are stained with the counterstain (red or brown).

Gram-positive, bacteria that are not decolorized when stained by Gram's method. They retain the original violet color of the Gram stain and are not stained by the counterstain.

Gram's method, a method of differential staining devised by Hans Gram, a Danish bacteriologist.

Granulation tissue, a youthful tissue composed of connective tissue cells and thin-walled blood vessels. It plays an important part in the healing of wounds and forms scar tissue.

Granulocyte, a granular leucocyte (polymorphonuclear neutrophile, eosinophile, or basophile).

Granuloma, a circumscribed collection of tissue resembling granulation tissue surrounding a point of irritation.

Gumma, a granuloma found in the late stages of syphilis.

"H" Agglutinins—see page 260.

Habitat, the place where a plant or animal is found in nature.

Heat stroke, a syndrome of headache, vertigo, slight delirium, and fever caused by exposure to an excessively high temperature.

Hectic fever, a daily recurring fever characterized by chills, sweating, and flushed countenance.

Hematemeses, the vomiting of blood.

Hematogenous, originating in the blood or borne by the blood.

Hematoma, a circumscribed effusion of blood.

Hematuria, the presence of blood in the urine.

Hemiplegia, paralysis of one side of the body.

Hemoglobinuria, the presence of hemoglobin in the urine.

Hemolysin, an antibody which in the presence of complement brings about the dissolving of red blood cells.

Hemolysis, the dissolving of red blood cells.

Hemolytic, having the power to cause hemolysis.

Hemophilia, a hereditary blood dyscrasia, due to a defect in the clotting mechanism, characterized by a tendency to profuse and long-continued hemorrhage. It affects only males and is transmitted only by females.

Hemoptysis, bleeding from the lungs or bronchial tree.

Hepatitis, inflammation of the liver.

Hepatogenous, arising in the liver.

Hereditary, transmitted through the members of a family from generation to generation.

Hernia, the protrusion of an organ or part of an organ through the wall of the cavity that contains it. The most common type of hernia is the protrusion of an abdominal viscus through the abdominal wall.

Heterologous, derived from an animal of another species.

Heterophile, having affinity for antigens or antibodies other than the one for which it is specific.

Homologous serum jaundice, a type of jaundice following the administration of human serum.

Hormone, a chemical that is formed in one part of the body and carried by the blood to another part or organ which it stimulates to functional activity.

Host, the animal or plant upon which a parasite lives.

Hydrarthrosis, a collection of fluid in a joint.

Hydration, the act of combining with water.

Hydrocele, a collection of fluid in a sacculated cavity; specifically in the tunica vaginalis testis.

Hydrocephalus, a condition, usually of congenital origin, characterized by an accumulation of fluid in the cerebral ventricles, dilatation of the ventricles, thinning of the brain, separation of the cranial bones, and enlargement of the head.

Hypdrops (see dropsy).

Hydrosalpinx, the accumulation of serous fluid in the fallopian tube.

Hydrothorax, the collection of a noninflammatory serous fluid in the pleural cavity.

Hyperactivity, an activity greater than normal.

Hyperchlorhydria, the presence of an excess of hydrochloric acid in the gastric juice.

Hyperchromic, containing more than a normal amount of pigment. Refers especially to red blood cells.

Hyperemia, congestion. The presence of an increased amount of blood in a part.

Hyperplasia, an increase in the size of a part brought about by an inflammatory condition.

Hypersecretion, an excessive secretion.

Hypersensitiveness, abnormal sensitiveness or sensibility.

Hyperthyroidism, a train of symptoms brought about by an excessive activity of the thyroid gland or the taking of too much thyroid extract.

Hypertrophy, an increase in the size of an organ brought about by an increase in the functional demands made upon it.

Hypha; pl. *hyphae*, one of the filaments composing a fungus.

Hyphomycetes, pathogenic molds.

Hypochlorhydria, a deficiency in the hydrochloric acid of the gastric contents.

Hypochromic, containing less than the normal amount of coloring matter. Refers especially to red blood cells.

Hypostatic congestion, stagnation of the blood in the lower parts of the body due to weakness of heart action and the effects of gravitation. Most often seen in the dorsal portion of the lungs of persons who have been in bed for a long time.

Hypothyroidism, a train of symptoms caused by insufficient activity of the thyroid gland.

Hysterectomy, the surgical removal of the uterus.

Icterus, jaundice.

Ileocolitis, inflammation of the mucous membrane of the ileum and colon.

Ileum, the third or last portion of the small intestine.

Immune, exempt from a given infection.

Immune bodies, antibodies.

Immune serum, a serum containing immune bodies.

Immunity, a natural or acquired resistance to a disease.

Immunologist, one versed in immunity.

Immunology, the science which deals with immunity.

Impaction, the process of being closely packed together.

Impair, to lessen in quality or quantity.

Impetigo contagiosa, an infectious vesicular and pustular eruption most often seen on the faces of children.

Implantation, to add to or plant upon.

Inanimate, without life.

Incipient, just beginning.

Incompatible, not capable of being mixed without undergoing destructive chemical changes or acting antagonistically.

Incompetency, incapability of performing the required work. An incompetent heart valve is one that does not close completely, allowing the blood to leak back through it when the chamber in front of it contracts.

Incontinence, inability to prevent the discharge of the body excretions, particularly urine and feces.

Incoordination, lack of harmonious muscular action.

Incubate, to promote the growth of microorganisms by placing them in an incubator.

Incubation period, the period intervening between the time of infection and the appearance of the symptoms of a disease.

Incubator, a cabinet in which a constant degree of temperature is maintained for the purpose of growing cultures of bacteria.

Indicator, something which renders visible the completion of a reaction.

Indirect contact, the transfer of infection by means of inanimate objects, contaminated fingers, water, food, etc.

Induration, the act of hardening. A spot of hardened tissue.

Infection, invasion of the body by pathogenic agents with their subsequent multiplication and the production of disease.

Infectious, capable of being transmitted by the process of infection.

Infectious granuloma, a granuloma due to infection.

Infectious hepatitis, an epidemic type of hepatitis thought to be caused by a virus.

Infestation, invasion of the body by macroscopic parasites.

Infiltration, the act of penetrating between the cells composing a tissue.

Inflammation, a protective reaction on the part of the tissues brought about by the presence of an irritant.

Ingestion, the process of taking into the stomach.

Ingress, entrance.

Inhalation, inspiring or drawing in the breath.

Inhibition, a diminution or arrest of function.

Inoculate, to introduce artificially a disease-producing agent into the body.

Inoculation, the process of inoculating.

Inspissate, to thicken by evaporation or the absorption of fluid.

Insufficiency (see incompetency).

Insulin, a principle arising in the islands of Langerhans of the pancreas which controls carbohydrate metabolism.

Intercurrent infection, an infection that attacks a person already ill of another disease.

Interepidemic, between epidemics.

Intermittent, characterized by periods of activity separated by periods of quietude.

Intermittent sterilization (see fractional sterilization).

Interstitial, relating to spaces or interspaces in a structure.

Intoxication, poisoning.

Intracellular, within a cell.

Intracranial, within the skull.

Intracutaneous (see intradermal).

Intradermal, within the substance of the skin.

Intraperitoneal, within the peritoneal cavity.

Intraspinal, within the vertebral canal.

Intrauterine, within the uterus.

Intravenous, within a vein.

Intussusception, the infolding of one segment of intestine into another.

Invagination, the passage of one part into another part of the same thing.

Involution forms, abnormal forms assumed by microorganisms growing under unfavorable conditions.

Ionization, the dissociation into ions that occurs when an electrolyte is dissolved.

Iritis, inflammation of the iris (the diaphragm in the anterior portion of the eye which is perforated by the pupil).

Ischemia, local anemia caused by obstruction of the arterial supply of a part.

Isolate, to close all avenues by which a person may spread infection to others. To separate from others.

Karyosome (see caryosome).

Keratitis, inflammation of the cornea.

Koch's postulates or Koch's laws, a statement of certain requirements that must be met before a given microorganism can be considered the cause of a certain disease.

Lacerate, to tear.

Laceration, a lacerated (torn) wound.

Lactation, the production of milk.

Lactiferous, conveying milk. Ex.—the lactiferous ducts of the breast.

Lactose, grape sugar $C_{12}H_{22}O_{11}$.

Languor, lack of energy. Weakness.

Larva; pl. *larvae*, the young of any animal differing in form from its parent.

Lesion, the specific pathological change brought about by a disease.

Leucemia, leukemia, a marked and permanent increase in leucocytes due to an underlying disease of the leucocyte-producing tissues.

Leucocidin, a substance which destroys leucocytes.

Leucocyte, a white blood cell.

Leucocytosis, a transient protective increase in leucocytes brought about in response to an injury.

Leucopenia, a decrease in leucocytes.

Leucoplakia, a condition characterized by the occurrence of irregular white patches on the tongue and inside of the cheek.

Lipase, a fat-splitting enzyme.

Lithopedion, a calcified fetus. A stone child.

Lobulated, divided into lobules.

Lobule, an irregular or rounded part. One of the subdivisions of an organ or part bounded by some kind of structural demarcation.

Local infection, one that is confined to a restricted area.

Lumbar, the part of the back between the ribs and pelvis.

Lumen, the space inside a tubular structure.

Lumpy jaw, actinomycosis in cattle.

Lymphadenitis, inflammation of a lymph node.

Lymphadenopathy, enlargement of a lymph node.

Lymphocyte, a nongranular white blood cell of lymphoid origin.

Lymphocytosis, an increase in lymphocytes.

Lymphoid tissue, a tissue composed of a connective tissue framework supporting lymphocytes.

Macrocytic, characterized by the presence of abnormally large cells.

Refers especially to red blood cells.

Macroscopic, visible to the naked eye.

Macular, consisting of small spots differing in color from the surrounding tissue.

Malignant, not benign. A malignant tumor is one that infiltrates the surrounding tissues, spreads to distant parts of the body, has a tendency to recur after removal, and untreated always causes death.

Mechanical transfer (of infection), referring to the transfer of infection by insects in which the infectious material is transferred mechanically instead of undergoing a cycle of development in the body of the insect accomplishing the transfer.

Medulla, a marrow-like structure, especially in the center of a part, Ex.-bone marrow.

Medullary cavity, a marrow cavity; i. e., the cavity of a bone.

Membranous croup, a lay term indicating diphtheria.

Meninges, the membranes covering the brain and spinal cord.

Meningitis, inflammation of the meninges.

Menopause, termination of the menstrual life.

Menorrhagia, excessive menstrual flow.

Mesentery, a double layer of peritoneum attached to the abdominal wall and covering or enclosing in its folds a portion or all of one of the abdominal viscera conveying to it the vessels and nerves.

Metabolism, the sum total of the chemical changes whereby the nutrition and functional activities of the body are maintained.

Metachromatic granules, granules of deeply staining material found in certain bacteria.

Metastasis, the spread of a disease from a primary focus to distant parts of the body. In malignant tumors the appearance of secondary growths in parts of the body at a distance from the primary growth.

- Metastatic**, relating to metastasis.
- Metazoa**, multicellular animals.
- Metrorrhagia**, excessive bleeding from the uterus not associated with menstruation.
- Microbe**, a unicellular organism, either animal or plant.
- Microbiology**, the science that treats of microbes.
- Microcytic**, characterized by the presence of cells of less than normal size. Refers especially to red blood cells.
- Micromillimeter**, one thousandth part of a millimeter or 1-25,000 of an inch. A micron.
- Micron** (see micromillimeter).
- Microorganism**, an animal or plant of microscopic size.
- Microscopy**, the study of objects by means of the microscope.
- Miliary**, resembling a millet seed in size. Miliary tuberculosis, acute, more or less generalized tuberculosis.
- Minimum lethal dose**; abbr. *M.L.D.*, the smallest dose that will cause death.
- Misnomer**, a name wrongly used.
- Mitosis**, indirect cell division.
- Mixed culture**, a culture containing two or more kinds of organisms.
- Mixed infection**, an infection with two or more kinds of organisms.
- Mixed vaccine**, a vaccine containing two or more kinds of organisms.
- Molds**, a division of the group of organisms known as fungi.
- Mole**, a nevus. A mass formed by the degeneration of the partly developed ovum.
- Monarticular**, relating to a single joint.
- Mordant**, a chemical added to a dye to make it stain more intensely.
- Morphological**, pertaining to shape or form.
- Mucoid**, resembling mucus.
- Mucosa**, the mucous membrane.
- Multicellular**, composed of many cells.
- Multipara**; pl. *multiparas*, a woman who has given birth several times.
- Murmur**, a soft blowing sound most often due to a heart lesion.
- Mycelium**, the vegetative part of a fungus, consisting of many hyphae.
- Mycobacterium**, a genus of bacteria to which the tubercle bacillus belongs.
- Mycology**, the science which deals with fungi.
- Mycosis**, a disease caused by fungi.
- Myocarditis**, inflammation of the myocardium.
- Myocardium**, the muscular layer of the heart wall.
- Myxedema**, a disorder due to deficient action of the thyroid gland characterized by edema of the subcutaneous tissues, dryness of the skin, loss of hair, subnormal temperature, and slow heart action.
- Naris**; pl. *nares*, nostril.
- Nasopharynx**, the portion of the pharynx above the palate.

Natural immunity, an immunity with which a person or animal is born.

Necrosis, death of a mass of tissue while yet a part of the body.

Negri bodies, minute bodies found in certain cells of the brain of an animal with rabies.

Neoplasm, a tumor.

Neuralgia, a severe throbbing pain distributed along the course of a nerve.

Neuritis, inflammation of a nerve.

Neurosyphilis, syphilis affecting the central nervous system.

Night blindness, imperfect vision or blindness at night or in a dim light, with good vision on bright days.

Nitrogenous, relating to or containing nitrogen.

Nocturnal, occurring during the night.

Nodular, characterized by the presence of nodules.

Nodule, a small circumscribed mass of tissue; a small node.

Nonpathogenic, not productive of disease.

Normoblast, a nucleated red blood cell of normal size.

Normochromic, containing a normal amount of coloring matter.
Refers especially to red blood cells.

Normocyte, a normal red blood cell.

Normocytic, characterized by the presence of cells of normal size.
Refers especially to red blood cells.

Nucleolus; pl. *nucleoli*, a body within the nucleus of a cell which takes part in the metabolic process of the cell and plays a part in its multiplication.

Nucleus; pl. *nuclei*, the central, compact portion of a cell that is the functional center of the cell.

Obese, extremely fat.

Occlude, to close up.

Occult, concealed. Not discernible to the senses. Ex.—occult blood: blood that can be detected only by chemical tests.

Old tuberculin; abbr. *O.T.*, a special type of tuberculin.

Oliguria, a decrease in the amount of urine excreted.

Omentum, a single or double fold of peritoneum passing from the stomach to another abdominal organ.

Opalescent, resembling an opal in the display of colors.

Opportunists, bacteria that produce infection only under especially favorable conditions.

Opposing, acting against.

Opsonins, substances in the blood that render microorganisms more susceptible to the action of phagocytes.

Optimum temperature (as applied to bacterial growth), the temperature at which bacteria grow best.

Organ, a part of the body that performs a specific function or functions.

Organelle, a specialized part of a protozoon which performs a special function.

Organism, a living being, either animal or vegetable.

Organization, the assumption of a structural form.

Osmosis, the passage of fluids or other substances through a membrane.

Ossification, the change of a tissue into bone.

Osteitis, inflammation of bone.

Osteochondritis, inflammation of bone with its cartilage.

Osteogenic, producing bone.

Osteomyelitis, inflammation of the bone marrow.

Otitis media, inflammation of the middle ear.

Paleontology, the science which treats of prehistoric life.

Pallor, paleness.

Palpate, to examine by feeling.

Pancreatitis, inflammation of the pancreas.

Pandemic, a very widespread epidemic.

Papilloma, a circumscribed outgrowth from the skin or mucous membrane. **Ex.**—a wart.

Parasite, an animal or vegetable organism that lives on another.

Parenchyma, the specialized functioning tissue of an organ.

Parenchymatous, pertaining to the parenchyma.

Parenterally, in some manner other than by the intestinal tract.

Parietal, relating to the wall of a cavity.

Paroxysm, a sudden attack of a disease or acceleration of the symptoms of an existing disease.

Particulate, existing as minute separate particles.

Parturient, relating to or being in the process of childbirth.

Passive carrier, a carrier who harbors the causative agent of a disease without having had the disease.

Passive immunity, an immunity brought about without the body of the person or animal that becomes immune taking any part in its production. **Ex.**—the production of an immunity to diphtheria by the injection of diphtheria antitoxin.

Pasteurization, the heating of milk, etc., to a low temperature for a short time whereby pathogenic bacteria are destroyed but the food properties and flavor of the material are not affected.

Pathogenic, capable of causing disease.

Pathognomonic, characteristic or indicative of a disease.

Pathogenicity, disease-producing qualities.

Pedicle, a stalk or stem by which a tumor is sometimes attached to the structure from which it arises.

Pedunculated, attached by a pedicle.

- Pepsin**, a digestive enzyme, occurring in the gastric contents, which digests proteins.
- Pericardium**, the saclike structure surrounding the heart.
- Perineum**, the area lying between the vulva and anus in the female and between the scrotum and anus in the male.
- Periosteum**, the thick fibrous membrane covering the surface of a bone.
- Periostitis**, inflammation of the periosteum.
- Peripheral**, related to or situated at the periphery.
- Periphery**, the outer part or surface of the body.
- Periproctitis**, inflammation of the tissue about the rectum.
- Perirectal**, surrounding the rectum.
- Peritoneum**, the serous membrane which lines the abdominal walls and invests the abdominal viscera.
- Peritonitis**, inflammation of the peritoneum.
- Permanent carrier**, a carrier that harbors a disease-producing agent for months or years.
- Permeability**, the state or quality of being permeable; i. e., may be passed through, as a porous membrane.
- Petechia**; pl. *petechiae*, pinpoint hemorrhages into the skin.
- Petechial**, relating to or accompanied by petechiae.
- Petri dish**, a round glass dish with cover used for growing bacterial cultures.
- Peyer's patches**, collection of lymphoid nodules packed together to form oblong elevations of the mucous membrane of the small intestine, their long axis corresponding to that of the intestine.
- Phagedena**, a widespread sloughing ulcer.
- Phagocyte**, a cell capable of ingesting bacteria or other foreign particles.
- Phagocytic**, related to phagocytes or phagocytosis.
- Phagocytosis**, the process of ingestion by phagocytes.
- Phenol coefficient**, the disinfecting property of a chemical as compared with that of phenol (carbolic acid).
- Phlegmon**, an acute suppurative inflammation of the subcutaneous connective tissue.
- Phlyctenular**, characterized by the formation of vesicles (small blisters).
- Photosynthesis**, the construction of glucose from carbon dioxide and water by sunlight in the presence of chlorophyl.
- Pia mater**, the inner of the three layers of meninges covering the brain and spinal cord.
- Plasma**, the fluid portion of the circulating blood. The fluid portion of clotted blood is known as serum.
- Plasmolysis**, the shrinking of a cell when suspended in a hypertonic solution.
- Plasmoptysis**, the swelling and bursting of a cell when suspended in a hypotonic solution.

- Plastids**, small bodies found in the cytoplasm of cells. They have to do with cell nutrition and contain the chlorophyl of green plants.
- Pleomorphism**, the existence of different forms in the same species.
- Pleurisy**, inflammation of the pleura.
- Plexus**, an interlacing network of nerves, veins, or lymphatics.
- Polar bodies**, deep staining bodies found in one or both ends of certain species of bacteria.
- Pollution**, to render unclean. As used in bacteriology, to render unclean by adding harmful bacteria.
- Polyp** (see *polypus*).
- Polypus**, a pedunculated swelling or outgrowth springing from a mucous membrane.
- Polyuria**, excessive excretion of urine.
- Portal**, a place of entrance.
- Postnatal**, occurring after birth.
- Potency**, power, force, strength.
- Precancerous**, preceding the appearance of a cancer.
- Precipitation**, the process of clumping of proteins in solution caused by the addition of a specific precipitin.
- Precipitins**, antibodies that cause precipitation.
- Predisposing**, rendering more vulnerable.
- Prehension**, taking hold of, grasping.
- Preservative**, a substance which is added to a product for the purpose of preventing bacterial growth and consequent spoiling.
- Primary infection**, the first of two infections, one occurring during the course of the other.
- Primary take**, the ordinary reaction following the vaccination of a person not immune to smallpox.
- Proctitis**, inflammation of the rectum.
- Prognosis**, a forecast of the outcome of a disease.
- Prognostic**, relating to prognosis.
- Prophylactic**, relating to prophylaxis.
- Prophylaxis**, the prevention of disease.
- Prostration**, great depression of vital activities.
- Protoplasm**, the living material of which cells are composed.
- Protozoology**, the science which treats of protozoa.
- Protozoon**; pl. *protozoa*, a unicellular animal organism.
- Proud flesh**, an unhealthy fungous growth of granulation tissue which protrudes from a wound and shows no tendency to undergo scar formation.
- Pseudomembrane**, a fibrinous exudate forming a tough membranous structure on the surface of the skin or mucous membrane.
- Pseudomucin**, a protein resembling mucin found in certain cysts, especially those of the ovary.
- Pseudopod**, a temporary protoplasmic process put forth by a protozoon for purposes of locomotion or obtaining food.

Psoas abscess, an abscess in the sheath of the psoas major muscle.
Such an abscess is usually the result of tuberculosis of the spinal column and usually points on the inner side of the thigh.

Psychic, relating to the mind.

Psychosis, a disorder of the mind.

Ptomaines, basic substances resembling alkaloids formed during the decomposition of dead organic matter.

Pure culture, a culture containing only one species of organism.

Purgative, cathartic.

Purulent, containing pus.

Pus, a fluid product of inflammation consisting of liquid, derived from the blood plasma, leucocytes, bacteria, dead cells, and foreign elements.

Pustule, a circumscribed elevation on the skin containing pus.

Putrefaction, the decomposition of proteins.

Pyelitis, inflammation of the kidney pelvis.

Pyemia, a form of septicemia in which the organisms in the blood stream lodge in the organs and tissues and set up secondary foci of suppuration.

Pylorus, the opening leading from the stomach to the small intestine.

Pyogenic, pus forming.

Pyosalpinx, a collection of pus in a fallopian tube.

Quiescent, not active.

Racial immunity, an immunity peculiar to a race.

Radiation, treatment by radium or x-ray.

Radio-sensitive, a quality possessed by cells or tissues which renders them easily injured or destroyed by radiation.

Rarefaction, the process of becoming less dense.

Raw, as applied to milk, not pasteurized.

Reaction of immunity, a reaction indicating that a person is immune to the substance causing the reaction. Particularly applied to the reaction of a smallpox-immune person following smallpox vaccination.

Receptors, a term used by Ehrlich in his side-chain theory of immunity to denote specialized portions of the cell which combine with foreign substances, such as foods, toxins, etc.

Recumbent, lying down.

Recurrent, characterized by recurrence of symptoms after an intermission.

Regeneration, the reproduction of lost parts.

Regurgitate, to expel the contents of the stomach in small amounts.

Remission, a temporary cessation of the symptoms of a disease.

Remittent, characterized by remissions.

Renal, relating to the kidneys.

Renal diabetes, a disease characterized by the escape of sugar into the urine without an increase in blood sugar.

Rennin, a milk-curdling enzyme found in the gastric juice.

Resection, the removal of a portion of an organ.

Resistance, the power of the body to ward off disease.

Resolution, the arrest of an inflammatory process without the formation of pus. The removal of the products of inflammation.

Reticuloendothelial system, a system of cells scattered through various organs and tissues, particularly the spleen, liver, and bone marrow. It seems to play an important part in immunity.

Retraction, to draw back or in.

Retropharyngeal, behind the pharynx.

Rickets, a deficiency disease of young children characterized by softening of the bones, enlargement of the liver, profuse sweating, and general tenderness.

Ringworm, a fungus disease of the skin.

Rodent, a gnawing mammal (rats, mice, etc.).

Romberg's sign, swaying of the body when the subject stands with his feet together and his eyes closed.

Rose spots, characteristic spots that occur over the lower portion of the trunk and abdomen in typhoid fever.

Rudimentary, imperfectly developed.

Ruga; pl. *rugae*, a fold, ridge, or wrinkle.

Saccharomyces, nonpathogenic yeasts.

Salivation, an excessive secretion of saliva.

Salpingitis, inflammation of the fallopian tube.

Sanitary, conducive to health.

Sapremia, a condition in which the products of the action of saprophytic bacteria on dead tissues, such as retained placentas or gangrenous limbs, are absorbed into the body and produce disease.

Saprophyte, an organism that normally grows on dead matter.

Saprophytic, relating to a saprophyte.

Schick test, a skin test to detect susceptibility to diphtheria.

Sciatica, neuralgia of the sciatic nerve.

Scrofula, tuberculosis of the lymph nodes, particularly those of the neck.

Secondary infection, an infection occurring in a host already suffering from an infection.

Sedentary, not active.

Sedimentation, the formation of a sediment.

Selective action, the tendency on the part of disease-producing agents to attack certain parts of the body.

Sensitization, the process of rendering sensitive.

Sepsis, poisoning by the products of putrefactive processes.

Septic, relating to or caused by the presence of pathogenic organisms or their toxins.

Septicemia, a systemic disease caused by the invasion of the blood stream by pathogenic organisms, with their subsequent multiplication.

Septum; pl. *septa*, a thin wall dividing two cavities.

Sequence, results; order of succession.

Sequestrum, a portion of dead bone which has become separated from the healthy bone.

Serological, relating to serology.

Serology, that branch of science which deals with serums, especially immune serums.

Serous surface, the surface of one of the smooth membranes lining one of the closed cavities of the body.

Serum, the fluid that exudes when the blood coagulates. Fluid poured from the blood vessels into the tissues or upon a surface as a result of inflammation.

Serum sickness, a train of symptoms occurring eight or ten days after the injection of the serum of a different species. Important among these symptoms are urticaria, painful joints, fever, and swelling of the lymph nodes.

Sessile, having a broad base of attachment.

Shock, a state of severe mental and physical depression following physical injury or emotional disturbance.

Sinuuous, bending in and out in a wavy manner.

Sinus, a tract leading from an area of infection to the surface. A channel for the passage of blood which does not have the same coats in its wall as an ordinary blood vessel.

Sinus thrombosis, thrombosis of a sinus.

Skin test dose; abbr. *S.T.D.*, the unit of measurement of scarlet fever toxin, the amount required to produce a positive reaction on the skin of a person susceptible to scarlet fever.

Slough, a separation of dead tissue from the living tissue.

Smear, a very thin layer of material spread on a glass slide.

Species immunity, an immunity peculiar to a species.

Specific gravity, the weight of a substance as compared with the weight of an equal volume of distilled water.

Spermatic cord, a cord formed by the vas deferens and its accompanying vessels and nerves.

Spherule, a small sphere.

Sphincter, a circular muscle which serves to close a body orifice.

Spina bifida, a defect of the spinal column characterized by the absence of one or more vertebral arches with protrusion through the opening of the spinal membranes and in some cases both membranes and spinal cord.

Spirilla; sing. *spirillum*, bacteria of a corkscrew shape.

Splenic, relating to the spleen.

Spontaneous, occurring without external stimulation.

- Spontaneous generation**, a theory which held that microorganisms arose spontaneously.
- Sporadic**, occurring separately or apart from others of its kind.
- Sporadic disease**, a disease that occurs sporadically; i. e., neither endemic nor epidemic.
- Spore**, a highly resistant form assumed by certain species of bacteria when grown under adverse influences. The reproductive cells of certain types of organisms.
- Sporulation**, production of spores or division into spores.
- Stain**, a dye used in bacteriological and histological technic.
- Staining**, coloring cells or tissues with stains.
- Staphylococci**; sing. *staphylococcus*, cocci that occur in irregular grape-like clusters.
- Status lymphaticus**, a condition of infancy and childhood characterized by hyperplasia of the lymphoid structures, persistence of the thymus, and a tendency toward sudden death.
- Stenosis**, narrowing or closure of a canal or passage.
- Sterile**, free of living microorganisms and their products.
- Sterilization**, the process of making sterile.
- Stock vaccine**, a vaccine made from cultures other than those from the patient who is going to receive the vaccine.
- Strangulation**, cutting off the air or blood supply by constriction.
- Streptococci**, cocci that divide in such a manner as to form chains.
- Stricture**, narrowing or closure of a tubular structure.
- Stroma**, the supporting framework of an organ or gland.
- Stupor**, unconsciousness.
- Subcutaneous**, beneath the skin.
- Subdural**, beneath the dura mater.
- Sulphur granules**, small yellow granules found in the pus from the lesions of actinomycosis.
- Sunstroke**, heat stroke due to the action of sun rays.
- Suppuration**, the formation of pus.
- Suppurative**, forming pus.
- Supraclavicular**, above the clavicle.
- Susceptibility**, the state or quality of being susceptible.
- Symbiosis**, the mutually advantageous association of two or more organisms.
- Symbiotic**, relating to symbiosis.
- Synovial membrane**, the lining membrane of a joint.
- Synovitis**, inflammation of a synovial membrane.
- System**, a group of organs concerned in performing the same general function. The entire organism.
- Systemic**, relating to a system. Relating to the entire organism instead of a part.
- Technic, technique**, the method of performing an operation, test, or other procedure.

Teratoma, a complex tumor whose tissues represent several different organs.

Terminal disinfection, disinfection of a room after it has been vacated by a patient.

Terminal infection, an infection with streptococci or other pathogenic bacteria that occurs during the course of a chronic disease and causes death.

Thallophytes, a division of the plant kingdom to which the fungi and bacteria belong.

Thermal death point, the degree of heat necessary to kill a liquid culture of a given species of bacteria in ten minutes.

Thrombosis, the formation of a thrombus.

Thrombus, a plug that more or less completely occludes a blood vessel or heart cavity formed in situ by coagulation of the blood or the deposit of some of its formed elements.

Tissue, a collection of cells forming a definite structure.

Tortuous, full of turns and twists.

Toxemia, the presence of toxins in the blood.

Toxin, a poisonous substance elaborated during the growth of pathogenic bacteria.

Toxin-antitoxin, a mixture of toxin and antitoxin containing a slight excess of the former, used to produce an active immunity.

Toxoid, toxin that has been treated in such a manner that its toxic properties are destroyed without affecting its antibody-producing properties.

Translocation, the transfer of food material in solution through the sieve tubes of vascular plants.

Transpiration, the exhalation of watery vapor from the stomata of plants.

Transudate, a noninflammatory collection of fluid.

Traumatism, a wound or injury.

Trichiniasis, **trichinosis**, a disease caused by the presence of the larvae of *Trichinella spiralis* in the muscles.

Tubercle, a nodule or group of nodules that forms the specific lesion of tuberculosis.

Tuberculin, a toxic extract obtained from tubercle bacilli.

Tuberculous, affected with tuberculosis.

Turbid, cloudy; not clear.

Turbidity, state or quality of being turbid.

Ulcer, a circumscribed area of necrosis of the skin, mucous membrane, or serous membrane.

Ulceration, the process of ulcer formation.

Unicellular, composed of but a single cell.

Unilateral, confined to one side.

Unit, a standard of measurement.

Vaccinate, to introduce a vaccine into the body.

Vaccination, the introduction of a vaccine into the body.

Vaccine, the causative agent of a disease so modified that it is incapable of producing disease while retaining its power to cause antibody formation.

Vacuole, a clear space in the substance of a cell.

Vaginitis, inflammation of the vagina.

Variation, deviation from the parent form.

Varix; pl. *varices*, an enlarged and tortuous vein, artery, or lymph vessel.

Vascular, containing blood vessels.

Vegetations, a growth or excrescence. A clot adherent to a diseased heart valve.

Vegetative bacteria, nonspore-forming bacteria or spore-forming bacteria in their nonsporing state.

Ventricle, a small cavity, especially of the heart or brain.

Vertigo, a sensation of going round and round either of oneself or of external objects.

Vesicle, a small circumscribed elevation of the skin containing a nonpurulent fluid.

Vesicular, relating to or associated with vesicles.

Vincent's angina, an ulcerated condition of the tonsils caused by a spirillum and fusiform bacillus.

Virus, a little understood agent of disease that has among others the following characteristics: (1) cannot be seen with the microscope, (2) cannot be propagated on nonliving media, and (3) passes through filters that retain all ordinary bacteria.

Virus neutralizing antibodies, antibodies which neutralize viruses.

Visceral, relating to the viscera.

Viscosity, the quality of being visced (thick, gelatinous).

Viscus; pl. *viscera*, an internal organ, especially one of the abdominal organs.

Vital, relating to life.

Vital functions, functions necessary for the maintenance of life.

Vitamins, certain little understood food substances whose absence leads to such deficiency disease as beriberi.

Wassermann test, the complement fixation test for syphilis devised by August von Wassermann.

Weil-Felix test, a nonspecific but highly valuable agglutination test for typhus fever in which the organism agglutinated is a member of the proteus group.

Wheal, a circumscribed elevation of the skin due to edema of the cutis vera.

Widal test, an agglutination test for typhoid fever.

Yeasts, a division of the organisms known as fungi.

Zoology, the science which treats of animal life.

INDEX

- A
- Abdominal adhesions, 688
 organs, early recognition of
 cancer, 565
 pregnancy, 716
 secondary, 717
- Abnormalities of body size, 571
- Abortion, tubal, 717
- Abscess, 497
 appendical, 670
 brain, 632
 cold, 515
 ischiorectal, 672
 of liver, 677
 psoas, 752
 retropharyngeal, 644, 752
- Accelerated reaction, 368
- Acetone bodies, 705
 in urine, 705
- Achlorhydria, 653
- Achondroplasia, 571
- Acid-fast bacteria, 104, 269
 diseases caused by, 512
 stain, 103
- Acidophilus milk, 175
- Acme of infectious diseases, 504
- Acquired immunity, 202
 syphilis, mode of infection, 393
- Acromegaly, 571, 744
- Actinomycosis, 409
- Action of antitoxins, 213
 of disinfectants, factors in-
 fluencing, 144, 145
 of sulfonamide compounds, 154
- Active carriers, 236
 hyperemia, 480
 immunity, 203
 therapeutic application, 203
- Activities of bacteria, 87
- Acuminate condyloma, 548
- Acute diseases, 452
 inflammation, 491
 yellow atrophy of liver, 676
- Adaptability of bacteria, 76
- Addison's disease, 746
- Adenocarcinoma, 558
- Adenoids, 615
- Adenoma, 549
- Adhesions, 499
 abdominal, 499, 688
- Adrenal glands, diseases of, 745
- Aerobes, 82
 facultative, 82
 obligate, 82
- Aerosol, 169
- African sleeping sickness, 425
- Agar plate method of standard-
 izing disinfectants, 147
- Age as cause of disease, 453
- Agents, bacteriostatic, 144
 carcinogenic, 543
- Agglutination, 194, 196
 discovery of phenomenon, 34
 diseases in which important, 197
 in identifying bacteria, 197
 tests, collecting blood for, 130
- Agglutinins, 195
 bacteria producing, 195
 group, 195
 immune, 195
 in human blood, 198
 nonspecific, 196
- Agglutinogens, 195
 in blood, 198
- Agranulocytic angina, 603
- Agranulocytosis, 603
- Air, disinfection of, 168, 169
 embolism, 488
 infections conveyed by, 233
 lack of, as cause of disease, 458
- Albinism, 572
- Albumin in urine, 704
- Albuminuria, 703
- Alcohol as disinfectant, 149
- Alcoholic beverages, distillation of,
 175
 manufacture of, 175
 cirrhosis of liver, 678
- Algae, 44
- Allergens, 222
- Allergic diseases, 222
- Allergy, 222, 225
 bacterial, 229
 desensitization in, 230
- Alpha-streptococci, 314
- Amboceptor, 194
- Amebiasis, 427
 laboratory diagnosis, 430
 mode of infection, 429
 prevention, 430
 source of infection, 429
- Amebic dysentery, 264, 427
- Ameboid motion, 63
- American Academy of Pediatrics,
 preventive inoculation,
 434
 contributors to science of micro-
 biology, 36
- Public Health Association, pre-
 ventive inoculation, 433

- Amitosis, 62
- Amyloid infiltration, 468
- Anaerobes, 82
 - facultative, 82
 - obligate, 82
- Anaerobic bacteria, culturing, 120
- Anal fissure, 673
- Anaphylaxis, 222, 223
 - following injection of immune serum, 227
 - passive, 223
 - theories of causes, 224
- Anatoxins, 92
- Anemia, 597
 - aplastic, 600
 - classification of, 597
 - erythroblastosis fetalis, 601
 - local, 482
 - of pregnancy, 600
 - pernicious, 599
 - primary, 597
 - secondary, 598
 - sickle cell, 601
- Aneurysm, 591
- Angina, Vincent's, 398
- Angiomas, 552
- Animal inoculation, 121
 - purposes of, 122
 - study of bacteria by, 107
 - life, lower forms of, 44
- Animals as conveyers of disease, 236
 - difference from plants, 42
- Ankylostoma, 665
- Anomalies, 571
 - of breast, 576
 - of central nervous system, 578
- Antagonism, 84
- Anthracosis, 470
- Anthrax, 348
 - bacillus, discovery of, 33
 - disposal of dead animals, 350
 - prevention, 349
 - specific therapy, 349
- Antibacterial serums, 215
- Antibiotics, 154
 - discovery of, 35
 - manufacture of, 177
- Antibodies, 191
 - against *E. typhosus*, 258
 - Ehrlich's side-chain theory of production, 192
 - heterophile, 198
 - kinds of, 192
- Antibody formation, immunity due to, 191
- Antigen, 191
- Antiscorbutic vitamin, 528
- Antiseptic action of soap, 147
 - surgery, origin of, 34
- Antiseptics, 144
 - common, 147
 - standardizing, 146
- Antitoxin, 92
 - diphtheria, 290, 293
 - first commercial production of, 34
 - unit of, 214
 - scarlet fever, 320
 - tetanus, 213, 299
 - unit of, 214
 - unit, 214
- Antitoxins, 194, 213
- Antivenins, 214
- Antixerophthalmic vitamin, 528
- Aplastic anemia, 600
- Apoplexy, 483, 591
- Appendical abscess, 670
- Appendicitis, 667
 - chronic, 671
 - leucocyte count in, 603
 - obliterative, 671
- Appendicular obstruction, 671
- Appendix, vermiform, 667
- Appert, François, discovery of canning, 32
- Apthous stomatitis, 641
- Argyria, 470
- Arnold sterilizer, 137
- Arrangement of bacteria, 67
- Arteries, diseases of, 590
- Arteriosclerosis, 590
- Arthritis, 755
 - gonorrheal, 758
 - tuberculous, 758
- Articles for public use, disinfection of, 168
- Ascaris lumbricoides, 666
- Aschheim-Zondek test for pregnancy, 742
- Ascites, 686
- ase, meaning of term, 88
- Asepsis, 144
- Asiatic cholera, 350
- Asphyxia, 458
- Asthma, 226
- Atelectasis, 618
- Atmospheric pressure, changes in, as cause of disease, 457
- Atrophy, 536
- Attenuation, 183
- Autoclave, description of, 139
 - operation of, 140
- Autogenous vaccines, 216
- Autopsy, 448
 - how to obtain, 448
 - laws relating to, 449
 - pathologist, 448
 - permit, 449
- Autotrophic bacteria, 80

Avenues by which bacteria enter
body, 181
leave body, 186
Avitaminosis, 527

B

B.C.G. vaccine, 281
Bacillary dysentery, 264, 512
cause, 264
mode of infection, 265
prevention, 265
Bacilli, 73
colon, 263
diphtheroid, 295
hemoglobinophilic, 341
Bacillus, anthracis, 348
characteristics of, 348
mode of infection, 348
botulinus (*see* Clostridium
botulinum)
definition of, 67
diphtheriae (*see* Corynebacterium
diphtheriae)
ducreyi, 345
influenzae (*see* Hemophilus in-
fluenzae)
leprae (*see* Mycobacterium
leprae)
mallei, 359
paratyphosus, 263
pertussus (*see* Hemophilus per-
tussis)
pyocyaneus (*see* Pseudomonas
pyocyaneus)
tetani (*see* Clostridium tetani)
tuberculosis (*see* Mycobacterium
tuberculosis)
typhosus (*see* Eberthella
typhosa)
Bacteria, 73
acid-fast, 104, 269
adaptability of, 76
aerobic, 82
anaerobic, 82
culturing, 120
and chlorophyl, 66
arrangement of, 67
autotrophic, 80
capsule, 69
causing infection, source of,
179
characteristics of, 66
chemical composition of, 66
classification of, 73
conditions affecting growth of,
79
counting by plating, 118
destruction by chemicals, 144
by natural methods, 142

Bacteria—Cont'd
determination of fermentation
reaction, 118
distribution of, 66
drug-fast, 77
effects of, 184
of boiling on, 82
of reaction of medium upon,
82
of temperature on, 80
entering body by digestive
tract, 181
by genitourinary tract, 181
by placenta, 181
by respiratory tract, 181
by skin, 181
fermentative action of, 89
food requirements of, 79
general effects of, 184
heat production, 93
how thrown off from body, 186
importance of, 66
in milk, 246
in processes of nature, 172
in urine, 706
intestinal, 667
leaving body by feces, 186
by mouth and nose, 186
by urine, 186
light production, 93
local effects of, 184
methods of studying, 96
mode of causing disease, 183
moisture requirement of, 80
motility of, 70
nitrifying, 174
nonpathogenic, 66
oxygen requirements of, 82
pathogenic, 66
pigment production of, 93
place among living things, 43
producing agglutinins, 195
exotoxins, 91, 285
production of odors, 93
relation to disease, 179
to other plants, 44
reproduction of, 71
requirements for best growth,
79
shape, 67
size of, 68
special activities, 87
spore formation, 71
sporulating, 72
structure of, 69
studying by immunological
methods, 205
types of infection produced by,
185

- Bacteria**—Cont'd
 unstained examination of, 96
 useful, 171
 variation of, 74
 vegetative, 72
- Bacterial allergy**, 229
 filtration, 135
 vaccines, preparation of, 216
 use, 216
 variation, 74
- Bactericides**, 144
- Bacteriemia**, 185
- Bacteriological diagnosis** of
 ulcerative lesions of
 throat, 131
 examination of water, 240
 incubator, description of, 54
- Bacteriology**, divisions of, 171
 father of, 29
- Bacteriolysins**, 194
- Bacteriophage**, 386
- Bacteriostasis**, 144
- Bacteriostatic agents**, 144
- Bacterium**, definition of, 67
tularense (*see* *Pasteurella tularensis*)
typhosum (*see* *Eberthella typhosa*)
- Baking**, 176
- Barlow's disease**, 534
- Bed linens**, disinfection of, 165
 sores, 474
- Beef tapeworm**, 665
- Benign tumors**, 546
 characteristics of, 546
 connective tissue, 550
 epithelial, 547
 transformation to malignant, 553
- Beriberi**, 533
- Beta-streptococci**, 314
- Bichloride of mercury** as disinfectant, 147
- Bile ducts**, diseases of, 679
 in urine, 705
- Biological classification**, principles of, 43
 names, 43
 transfer of disease, 235
- Birthmark**, 553, 572
- Black widow spider antivenin**, 214
- Bladder**, diseases of, 698
 exstrophy, 577
 stones, 699
 tumors, 699
- Blastomycosis**, 411
- Blood agglutinins**, 198
 agglutinogens, 198
- Blood**—Cont'd
 cells, 595
 red, 596
 white, 602
 color index, 597
 composition of, 595
 count, differential, 602
 cultures, collection of, 128
 in typhoid fever, 259
 for estimation of sulfonamide compounds, collecting, 130
 for serological examinations, collecting, 130
 groups, 198
 in feces, 661
 in stomach contents, 654
 in urine, 705
 platelets, 606
 poisoning, 185
- Boas-Oppler bacilli**, 654
- Bodies**, immune, 191
 inclusion, 364
 polar, 70
- Body defenses** against diseases, 461
 against infection, 189
 how bacteria enter, 181
- Boiling**, effects on bacteria, 82
 sterilization by, 137
- Boils**, 498
- Bone**, giant cell tumor of, 754
 tumors of, 752
 metastatic, 754
 primary, 754
 diseases of, 749
 tuberculosis of, 750
 syphilis of, 752
- Bordet-Gengou bacillus**, 343
- Boric acid** as disinfectant, 149
- Botulism**, 301
 antitoxin, 302
 symptoms of, 303
 prevention of, 303
- Bovine tuberculosis**, 271
- Brain abscess**, 632
 cerebrospinal fluid in, 638
 compression, 627
 concussion, 626
 embolism, 630
 encephalitis, 631
 hemorrhage, 630
 hydrocephalus, 628
 injuries, 626
 tumors, 634
 cerebrospinal fluid in, 638
- Branches of microbiology**, 42
- Breast**, carcinoma of, 727
 cysts of, 729

- Breast—Cont'd
 diseases of, 725
 early recognition of cancer of, 565
 malformations of, 576
 Bright's disease, urine in, 708
 Brill's disease, 389
 Broder's classification of cancers, 563
 Bronchi, 616
 dilatation of, 617
 inflammation of, 616
 Bronchiectasis, 617
 Bronchitis, 616
 Broncholiths, 471
 Bronchopneumonia, 305, 508
 complications of, 509
 leucocytes in, 509
 Brownian motion, 71, 98
 Brucella abortus, 357
 characteristics of, 357
 melitensis, 357
 mode of infection, 358
 pathogenicity, 358
 source of infection, 358
 suis, 357
 types, 357
 Brucellosis, 357
 immunity, 359
 laboratory diagnosis, 358
 prevention, 359
 specific therapy, 359
 Bubonic plague, 351
 Buttermilk, 174

C

- Cadaveric changes after death, 477
 Calcification, 468
 Calcium infiltration, 468
 Calculi, renal, 470, 696
 vesical, 470, 699
 Cancer (*see also* Carcinoma)
 of abdominal origin, early recognition, 565
 of breast, 565, 727
 of intestines, 660
 of lip, 564, 643
 of lymph nodes, 612
 of mouth, 564, 643
 of ovary, 713
 of prostate gland, 735
 of rectum, 675
 of skin, 559, 564
 of stomach, 650
 gastric contents in, 654
 of tongue, 564, 643
 of uterus, 565, 722
 susceptibility of organs to, 558
 Cancers, classification, 558
 Canning, food, 253
 origin of, 32
 Capsule of tumors, 546
 Capsules of bacteria, 69
 Capillary hemangiomas, 552
 lymph angiomas, 553
 Carbohydrases, 88
 Carbohydrates, determination of fermentation reactions of bacteria on, 118
 Carbolic acid (*see* Phenol)
 Carbuncle, 498
 Carcinogenic agents, 543
 Carcinoma, 554 (*see also* Cancer)
 basal cell, 559
 simplex, 559
 Carcinomas, classification, 558
 Cardinal signs of inflammation, 492
 Cardiovascular syphilis, 524
 Care of microscope, 46
 Carriers, active, 236
 animal, 236
 convalescent, 236
 diphtheria, 288
 diseases spread by, 236
 human, 235
 in pneumonia, 308
 intestinal, 236
 oral, 236
 passive, 236
 typhoid fever, 258
 urinary, 236
 Caruncle, urethral, 701
 Caseation necrosis, 473, 515
 Casts, 692, 705
 Cataract, 574
 Catarrhal stomatitis, 641
 Catheters, sterilization of, 160
 Causes of anaphylaxis, theories of, 224
 of disease, 452
 of hemorrhage, 482
 Cavernous hemangioma, 552
 Cell, 59
 definition of, 61
 division, 62
 membrane, 60
 multiplication, 62
 nucleus, 61
 function, 61
 Cells, normal and tumor, 543
 phagocytic, 200
 shape of, 59
 size of, 59
 structure of, 60
 Cellular concept of disease, 450
 theory of immunity, 190

- Centrifuge, description of, 57
 Cerebral concussion, 626
 embolism, 630
 hemorrhage, 630
 thrombosis, 630
 Cerebrospinal fever, 334
 fluid, collection, 133
 in disease, 637
 in meningitis, 637
 normal, 636
 pathological changes in, 636
 meningitis, epidemic, 334
 Cervix of uterus, carcinoma (cancer) of, 722
 Chancre, 394
 of lip, 642
 Chancroid, 345
 Characteristics of bacteria, 66
 of malignant tumors, 554
 of milk-borne epidemics, 247
 of water-borne epidemics, 239
 Cheese, 175
 Chemical composition of bacteria, 66
 theory of immunity, 190
 treatment of microbial diseases, 153
 Chemicals, effect on bacteria, 83
 Chemotaxis, 83
 Chemotherapeutic agents, 153
 Children, smallpox vaccination, 367
 tumors in, 566
 Chloasma, 572
 Chloramines, 151
 Chlorinated lime, 151
 Chlorine as disinfectant, 150
 Chlorophyll, relation of to bacteria, 66
 Chlorosis, 600
 Chlorthymol as disinfectant, 153
 Cholangitis, 681
 Cholecystitis, 681
 Choleliths, 470
 Cholera, Asiatic, 350
 Chondromas, 552
 Choosing a disinfectant, 146
 Chorionepithelioma, 724
 Chromatin granules, 61
 Chromidia, 61
 Chronic infectious arthritis, 756
 inflammation, 491, 499
 Cilia, 64
 Ciliata, 64, 419
 Ciliates, 64
 intestinal, 430
 Circulation, distributions of, 480
 of unicellular organisms, 63
 Circulatory organs, diseases of, 584
 Cirrhosis of liver, 678
 Classes of stains, 100
 Classification of anemias, 597, 598
 of bacteria, 73
 of streptococci, 313
 Cleft palate, 575
 Clinical pathology, 441
 thermometers, disinfection of, 167
 Clostridium botulinum, 301
 antitoxin, 302
 toxin of, 302
 types of, 302
 tetani, characteristics of, 296
 distribution, 296
 pathogenicity, 297
 toxin production, 297
 Clothing, disinfection of, 165
 Cloudy swelling, 466
 Coagulation necrosis, 473
 Coagulase, 92
 Cocci, 73
 classification of, 68
 gram-negative, 328
 gram-positive, 305
 pyogenic, 305
 Coccidioidal granuloma, 412
 Coccus, definition of, 67
 Coefficient, phenol, 146
 Cold as cause of disease, 457
 effects on bacteria, 81
 Collection of blood for estimation
 of penicillin, 130
 of sulfonamide compounds, 130
 for serological examinations, 130
 of cerebrospinal fluid, 133
 of nose cultures, 131
 of peritoneal fluid for bacteriological examination, 133
 of pleural fluid for bacteriological examination, 133
 of pus for bacteriological examination, 132
 of smears for gonococci, 132
 of specimens, 126
 from conjunctiva, 133
 of sputum for examination, 130
 of throat cultures, 131
 of urine, 128
 Colloid degeneration, 467
 goiter, 737
 Colon bacilli, 263
 in water, significance of, 240

- Colon—Cont'd
 typhoid, group of organisms, 255
- Colonies, 112
 R-type, 75
 S-type, 75
- Color blindness, 579, 580
 index of blood, 597
- Commensalism, 84
- Commercial uses of bacteria, 174
- Common antiseptics, 147
 colds, 374
 disinfectants, 147
- Communicable disease, 180, 452
 how transmitted, 233
- Compensated heart lesions, 589
- Complement, 193
 fixation, 208
 discovery, 34
 principles of, 205
 test for gonorrhea, 332
 in syphilis, 397
- Complications of pneumonia, 506
- Compound solution of chlorine, 151
- Compression, cerebral, 627
- Concretions, 470
 characteristics of, 471
 due to sulfonamides, 472
 in feces, 661
 intestinal, 471
 prostatic, 471
- Concurrent disinfection, 165
- Conditions affecting growth of bacteria, 79
- Condyloma, acuminate, 548
 latum, 549
- Congenital defects of development, 455, 571
 of stomach, 646
 diseases, 456
 mixed tumors of kidney, 694
 syphilis, 395
- Congestion hypostatic, 481
- Conjunctiva, collecting specimens from, 133
- Connective tissue tumors, benign, 550
 malignant, 559
- Constitution, 452
- Contact, direct, diseases spread by, 233
 indirect, diseases spread by, 233
- Contagious disease, 180
- Contamination, 179
- Continued fever, 464
- Contraction of scars, 499
- Convalescent carriers, 236
 serum, 215
- Copper sulphate as disinfectant, 149
 treatment of water, 150
- Coronary disease, 590
- Corrosive sublimate (*see* Bichloride of mercury), 147
- Corynebacterium diphtheriae, 285
 bacteriological diagnosis, 289
 characteristics of, 285
 cultures for, 131
 mode of infection, 288
 pathogenicity, 287
 polar bodies in, 286
 source of infection, 288
 toxin of, 287
- Counterstains, 102
- Counting bacteria, 118
- Cowpox and smallpox, relation between, 31, 367
- Crede's method, 333
- Cretinism, 738
- Crisis, 504
- Cross-eye, 574
- Cultural methods, use of, 107
- Culture, 107
 media, 80
 adjusting reaction of, 109
 differential, 110
 dyes in, 109
 enriching, 109
 origin of, 33
 penicillin inhibiting, 111
 preparation of, 107
 selective, 110
 suitable for different bacteria, 111
 sulfonamide inhibiting, 111
 medium, 107
 mixed, 107
 pure, 107, 113
- Cultures for *Corynebacterium diphtheriae*, collecting, 131
 from blood, collection of, 128
 making, 112
 on persons taking penicillin, 127
 taking sulfonamide drugs, 127
 pure, methods of studying, 118
 obtaining, 114
 purposes of, 112
- Culturing, 107
 anaerobic bacteria, 120
- Curing tobacco, 177
- Cutaneous horns, 549
- Cyst formation of protozoa, 418
- Cystadenoma of ovary, 710
- Cystadenomas, 549
- Cystitis, 698
- Cystoscopes, sterilization of, 161

- Cysts, 567
 - nabothian, 719
 - of breast, 729
 - of neck, 575
 - of ovary, 710
- Cytolysins, 194

D

- Dairy products, manufacture of, 174
- Dakin's solution, 151
- Dark-field illumination, 98
- Dating of serums and vaccines, 219
- Deaf-mutism, 579
- Death, 473
 - cadaveric changes, 477
 - cellular, 473
 - point, thermal, 137
 - sign of, 476
 - somatic, 473
 - time of, 478
- Decay, 88
- Decompensated heart lesions, 589
- Defects of development, 571
- Defenses of body against disease, 461
 - against infection, 189
- Deficiencies, vitamin, 527
- Deficiency diseases, 454
- Definitive host, 662
- Degeneration, 466
 - colloid, 467
 - fatty, 467
 - hyaline, 467
 - mucoid, 467
 - red, 721
- Dengue fever, 381
- Deodorants, 144
- Dermatomycosis, 407
- Dermoid cysts of ovary, 713
- Description of bacteriological incubator, 54
 - of centrifuge, 57
 - of microscope, 46
 - of water bath, 55
- Desensitization to allergic conditions, 230
- Destruction of bacteria by mechanical means, 135
- Dextrose in urine, 704
- Diabetes insipidus, 708, 745
 - mellitus, 706, 707, 747
 - relation of pancreas to, 747
 - renal, 707
 - urine in, 706
- Diabetic gangrene, 476
- Diacetic acid in urine, 705
- Diaphragmatic hernia, 656
- Diarrheas of infants, 266
- Diathesis, 453
- Dick test in scarlet fever, 319
- Differential blood count, 602
 - culture media, 110
 - stains, 101
- Digestive system, diseases of, 641
 - tract, bacteria entering body by, 181
- Dilatation of heart, 584
- Diphtheria, 285, 519
 - antitoxin, 290, 293
 - first commercial production of, 34
 - unit of, 214
 - bacteriological diagnosis, 289
 - carriers, 288
 - complications of, 520
 - immunity in, 291
 - laryngeal, 288
 - mode of infection, 288
 - nasal, 288
 - pathology, 519
 - prevention, 294
 - preventive inoculation, 433, 434
 - Schick test in, 292
 - source of infection, 288
 - specific therapy, 293
 - toxin-antitoxin, 218, 291
 - toxoid, 218, 292
- Diphtheroid bacilli, 295
- Diplobacilli, 68
- Diplococci, 68
- Diplococcus gonorrhea (*see* Gonococci)
- meningitides (*see* Meningococcus)
- of pneumonia (*see* Pneumococcus)
- Direct cell division, 63
 - contact, diseases spread by, 233
- Discharges from mouth and nose, sterilization, 167
 - from nipple, 726
- Disease, 450
 - and functional changes, 451
 - and structural changes, 451
 - bacteria as cause, 179
 - biological transfer of, 235
 - causes of, 452
 - cellular concept, 450
 - communicable, 180
 - congenital, 456
 - defenses of body against, 461
 - endemic, 186
 - epidemic, 186
 - etiology, 452
 - exposure to, in relation to immunity, 204

Disease—Cont'd

immunological methods of diagnosis, 205

inherited, 455

lymph node deposits in, 462

manifestations of, 451

nature of, 450

pathogenesis of, 452

relation of bacteria to, 179

self-limited, 504

signs and symptoms, 451

sporadic, 186

Diseases, allergic, 222

caused by bacteria producing extracellular toxins, 519

by fungi, 407

by pneumococci, 305, 311

by protozoa, 419

by rickettsiae, 388

by spirochetes, 520

by staphylococci, 324

by streptococci, 315, 316, 504

deficiency, 454

followed by immunity, 190

of coronary arteries, 590

of digestive system, 641

of nervous system, cerebrospinal fluid changes, 637

of throat, tonsillitis, 644

of wine, 32

spread by animals, 236

by human carriers, 236

by insects, 234

by water, 239

transmitted by food, 237

by milk, 247

venereal, 328

Disinfectant, 144

action of alcohol, 149

of bichloride of mercury, 147

of chlorine, 150

of chlorthymol, 153

of copper sulphate, 149

of dyes, 153

of ferrous sulphate, 150

of formaldehyde, 152

of hydrogen peroxide, 149

of lime, 150

of mercuric iodide, 148

of mercuric iodide, 148

of mercuriochrome, 148

of merthiolate, 148

of nitric acid, 149

of phenol, 152

of potassium permanganate, 150

of protargol, 149

of silver nitrate, 149

Disinfectant, action—Cont'd

of sulphur dioxide, 152

of tincture of iodine, 152

of tricresol, 152

choosing, 146

Disinfectants, common, 147

factors influencing action, 145

mode of action, 144

qualities of, 145

standardizing, 146

by agar plate method, 147

by wet filter paper method, 146

Disinfection, 144

concurrent, 165

in infectious diseases, 164

of air, 168, 169

of articles for public use, 168

of bed linens, 165

of clinical thermometers, 167

of discharges from mouth, 167

from nose, 167

of eating utensils, 167

of excreta, 164

of feces, 166

of hands, 161, 165

of mucous membranes, 164

of operating room, 163

of shoes, 166

of soiled clothing, 165

of sputum, 167

of urine, 166

of wounds, 164

surgical, 158

terminal, 165, 168

Distillation of alcoholic beverages, 175

Distribution of bacteria, 66

Disturbances of circulation, 480

Diverticula of intestine, 654

Diverticulum, Meckel's, 654

Division, cell, 62

Divisions of bacteriology, 171

of microbiology, 42

Dose, minimum lethal, 213

provocative of allergen, 222

skin test, 214

Dressings, sterilization of, 159

Drinking water standards, 242

Droplet infection, 233

Dropsy, 484

Drug idiosyncrasies, 229

Drug-fast bacteria, 77

Dry gangrene, 474

heat sterilization, 141

Drying, food, 253

Ducrey's bacillus, 345

Duodenal ulcer, 649

Dwarfism, 571, 745

- Dyes as antiseptics, 153
 in culture media, 109
- Dysentery, amebic, 264, 427
 bacillary, 512
 bacilli, 264
 distribution in body, 265
 pathogenicity, 265
 types of, 264
- E
- Early microscopes, 29
- Eating utensils, disinfection of, 167
- Eberthella typhosa, 255
 characteristics of, 255
 distribution in body, 257
 formation of antibodies against, 258
 in feces, 257
 in gall bladder, 257
 in urine, 257
 mode of entering body, 256
 of leaving the body, 257
 of spreading, 257
 pathogenicity of, 256
- Ectoenzymes, 88
- Ectopic pregnancy, 716
- Ectoplasm, 61
- Edema, 483
 of heart disease, 484
 of kidney disease, 484
- Eelworm, 666
- Effects of bacteria, 183, 184
 of chemicals on bacteria, 83
 of electricity on bacteria, 83
 of light on bacteria, 82
 of pressure on bacteria, 84
 of products of growth on bacteria, 83
 of radium on bacteria, 83
 of ultraviolet light on bacteria, 82
 of x-ray on bacteria, 83
- Ehrlich's side-chain theory, 192
 theory of immunity, 190
- Elective localization, 183
- Electricity as a cause of disease, 458
 effect on bacteria, 83
- Electron microscope, 52
- Embolism, 487
 air, 488
 causes of, 487
 fat, 488
 of brain, 630
 results of, 487
- Embolus, 487
- Emotional state as a cause of disease, 455
- Emphysema, 617
- Empyema of gall bladder, 681
- Encephalitis, 631
 cerebrospinal fluid in, 638
 epidemic, 377
 epidemiology, 377
 types, 377
- Endameba histolytica, 427
 cysts, 428
 lesions produced by, 429
 life history of, 428
 mode of infection, 429
 source of infection, 429
- Endemic disease, 186
- Endocarditis, 587
- Endocervicitis, 718
- Endocrine glands, diseases of, 736
- Endoenzymes, 88
- Endogenous causes of disease, 452
 infection, 180
 pigmentation, 469
- Endometritis, 718
- Endoplasm, 61
- Endotheliomas, 561
- Endotoxins, 90
- Enlargement of lymph nodes, 609
 of prostate gland, 734
- Enriching material in culture media, 109
- Enzymes, 87
 characteristics of, 87
- Eosinophiles, 605
- Eosinophilia, 605
- Epidemic, cerebrospinal meningitis (*see* Epidemic meningitis)
 disease, 186
 encephalitis, 377
 meningitis, 509
 complications of, 509
 immunity in, 337
 laboratory diagnosis, 337
 leucocytes in, 509
 pathology, 509
 prevention, 338
 specific therapy, 334
 parotitis, 372
- Epidemics, milk-borne, 247
 water-borne, 239
- Epididymitis, 731
- Epilepsy, 633
- Epinephrine, 745
- Epithelial tumors, benign, 547
 malignant, 556
- Epitheliomas, 558, 559
- Epulis, 644
- Equine encephalomyelitis, 378
- Equipment of microbiologist, 46
- Ergotism, 414

Erysipelas, 321
 cause of, 321
 mode of infection, 321
 Erythroblastosis fetalis, 601
 Erythrogenic toxin, 315
 Esophagus, diseases of, 646
 stenosis of, 646
 tumors of, 646
 Estivo-autumnal malaria, 420
 Etiology of disease, 452
 Exciting causes of disease, 456
 Excreta, disinfection of, 164
 Excretion of unicellular organisms, 63
 Exogenous causes of disease, 452
 infection, 180
 pigmentation, 469
 Exophthalmic goiter, 741
 Exotoxins, 90
 Exposure to disease, relation to immunity, 204
 Extracellular toxins, bacteria producing, 91
 Extrauterine pregnancy, 716
 Extrinsic factors causing tumors, 641
 Exudate, inflammatory, 490
 kinds, 490
 purpose of components, 492
 Exudates, 484
 Eyes, color of, 574

F

Face, abnormalities of, 574
 Facies, Hippocratica, 477
 Factors influencing action of disinfectants, 145
 occurrence of infection, 182
 Facultative aerobes, 82
 anaerobes, 82
 parasites, 79
 saprophytes, 79
 Fallopian tubes, diseases of, 714
 tuberculosis of, 716
 Families, tuberculosis in, 276
 Farcy, 359
 Far-sightedness, 574
 Fastidium of disease, 504
 Fat embolism, 488
 necrosis, 685
 Father of bacteriology, 29
 Fatty degeneration, 467
 infiltrations, 467
 metamorphosis, 467
 of liver, 676
 Feces, 660
 bacteria leaving body by, 186
 blood in, 661
 collection of specimens, 132

Feces—Cont'd
 concretions in, 661
 cultures in typhoid fever, 259
 disinfection of, 166
 mucus in, 661
 Female organs of reproduction, diseases of, 710
 Femoral hernia, 656
 Fermentation, 87, 175, 407
 meaning of term, 88
 Pasteur's studies, 32
 reactions of bacteria, 89, 118
 Ferrous sulphate as a disinfectant, 150
 Fever, 463
 and pulse rate, 464
 classification of, 464
 continued, 464
 course of, 464
 dengue, 381
 in inflammation, 498
 intermittent, 464
 mechanism of, 463
 rat-bite, 398
 relapsing, 397
 remittent, 464
 rheumatic, 505
 Rocky Mountain spotted, 389
 stages of, 464
 temperature range, 464
 trench, 390
 typhoid, 510
 typhus, 388
 undulant, 357
 yellow, 380
 Fibrinolysin, 92, 315
 Fibrinous exudate, 491
 Fibroadenoma of breast, 726
 Fibroid phthisis, 518
 Fibroids, 719
 Fibroma, 550
 Fibromyoma of uterus, 719
 Field of operation, disinfection of, 163
 Filters, water, 243
 Filth, diseases of, 237
 Filtrable viruses, 364
 miscellaneous diseases caused by, 383
 Filtration, bacterial, 135
 Fingers as spreaders of infection, 234
 Fissure, anal, 673
 Fistula, 498
 rectal, 673
 Fistulas of neck, 575
 Fixation of complement, 208
 nitrogen, 174
 Fixing and staining bacteria, 99
 tissues, 444

- Flagella, 64, 71
 Flagellates, 64, 419
 intestinal, 430
 Flax, retting, 177
 Flies as spreaders of infection, 234
 Flukes, 667
 Focal infection, 185
 Fomites, 237
 Food accessory factors, 527
 as conveyer of disease, 237
 as source of infection, 237
 bacteriology of, 171, 252
 diseases transmitted by, 237
 infection, 252
 intoxication, staphylococcus, 253
 poisoning, 252
 preservation, 253
 requirements of bacteria, 79
 supply as cause of disease, 454
 Foreign bodies, reaction of tissues to, 500
 Formaldehyde as disinfectant, 152
 Fractional sterilization, 140
 Freckles, 571
 Friedlander's bacilli, 361
 Friedman's test for pregnancy, 742
 Fumigation, 144
 of rooms, 168
 Function of cell nucleus, 61
 Functional changes, 451
 Fungi, 44, 402
 diseases caused by, 407
 Furuncles, 498
 Furunculosis, 498
 Fusospirillary infections, 398

G

- Gall bladder, disease of, 679
 empyema, 681
 inflammation of, 681
 stones in, 470, 683
 Gamma-streptococci, 315
 Gangrene, 474
 diabetic, 476
 dry, 474
 gas, 300
 moist, 474
 senile, 476
 Gastric cancer, 650
 stomach contents in, 654
 contents, blood in, 654
 composition of, 651
 examination of, 651
 hyperchlorhydria, 653
 hypochlorhydria, 653
 ulcer, 648
 Gastric ulcer—Cont'd
 stomach contents in, 654
 Genera, 43
 General effects of bacteria, 184
 infection, 185
 paresis, 523, 633
 stains, 100
 Generalized inflammation, 491
 Generation spontaneous, theory of, 31
 Genitourinary tract, bacteria, entering body by, 181
 German measles, 371
 Germicides, 144
 Giant cell tumor, 561, 644, 754
 Gigantism, 571, 744
 Gingivitis, 641
 Glanders, 359
 Gliomas, 561
 Glossitis, 641
 Gloves, sterilization of, 159
 Goat fever (*see* Brucellosis)
 Goiter, 737
 Gonococci, 328
 action of sulfonamide compounds on, 154
 characteristics of, 328
 collecting smears, 132
 compared with meningococci, 335
 mode of spread, 330
 pathogenicity of, 330
 smears, 331
 Gonorrhea, economic importance, 332
 immunity in, 333
 laboratory diagnosis of, 331
 mode of infection, 330
 prevention of, 333
 social importance, 332
 source of infection, 330
 spread in body, 331
 Gonorrheal arthritis, 758
 Good disinfectants, qualities, 145
 Grading milk, 249
 Gram-negative bacteria, 103
 cocci, 328
 Gram-positive bacteria, 103
 cocci, 305
 Gram's method of staining, 101
 Granulation tissue, 496
 Granules, metachromatic, 70
 Granuloma, 500
 Graves' disease, 741
 Group agglutinins, 195
 Groups, blood, 198
 Growth requirements of bacteria, 79
 Gumma, 521

H

- H-agglutinins** in typhoid fever, 260
Hair, abnormalities of, 571
 fungus diseases of, 407
Hand brushes, sterilization of, 160
Hands as conveyers of disease, 234
 disinfection of, 161, 165
Hanging-drop method, 96
 preparations, 97, 98
 slide, description, 97
Harelip, 575
Hay fever, 226
Healing, detrimental effects of, 499
Heart, congenital defects, 577, 584
 disease, edema, 484
 dilatation, 584, 589
 hypertrophy, 584
 lesions, compensated, 589
 decompensated, 589
 malformations of, 577, 584
 murmurs, 587
 valves, insufficiency, 589
 regurgitation, 589
 valvular defects of, 588
 vegetations on valves, 587
Heat, action on spores, 82
 as cause of disease, 457
 effects on bacteria, 81
 production by bacteria, 93
 sterilization, 136
 dry, 137
 moist, 137
Hemangiomas, 552
Hematemesis, 483
Hematogenous jaundice, 680
Hematomas, 483
Hematuria, 705, 706
Hemoglobin, 596
 in urine, 705
Hemoglobinophilic bacteria, 341
Hemoglobinuria, 705
Hemolysin, 92, 194
Hemolysis, 483
Hemolytic anemia, 598
 jaundice, 681
Hemophilus influenzae, 341
 characteristics of, 341
 pertussis, characteristics of, 343
 diagnosis of, 343
 immunity, 344
 mode of infection, 343
 pathogenicity of, 343
Hemorrhage, 482
 brain, 630
 causes of, 482
Hemorrhage—Cont'd
 from stomach, 647
 in typhoid fever, 511
 kinds, 482
 names of different kinds, 483
 of stomach and lungs, differentiation, 647
 renal, 691
 results of, 483
Hemorrhagic exudate, 491
Hemorrhoids, 674
Hemothorax, 621
Hemp, retting of, 177
Hepatic cirrhosis, 678
Hepatitis, infectious, 382
Hepatogenous jaundice, 680
Hereditary causes of disease, 455
Heredity in tumors, 541
Hermaphroditism, 580
Hernia, 655
 kinds of, 656
 obstructed, 656
 reducible, 656
 strangulated, 656
Heterophile antibodies, 198
Heterotrophic bacteria, 80
Hippocratic facies, 477
History of microbiology, 29
Hodgkin's disease, 611
Homologous serum jaundice, 382, 681
Hookworms, 665
Host, 79
 definitive, 662
 intermediate, 662
How bacteria cause disease, 183
 enter body, 181
 reach body, 180
Human carriers, 236
Humoral theory of immunity, 190
Hutchinson's teeth, 523
Hyaline degeneration, 467
Hydrocele, 732
Hydrocephalus, 628
Hydrogen peroxide as a disinfectant, 149
Hydronephrosis, 696
Hydrophobia, 378
Hydrosalpinx, 713
Hydrothorax, 621
Hyperchlorhydria, 653
Hyperemia, 480
Hyperinsulinism, 747
Hypernephroma, 694
Hyperopia, 574
Hyperpituitarism, 744
Hyperplasia, 538
 of prostate gland, 734
Hyperplastic goiter, 737

Hypersensitiveness, 222
 tests for, 230
 to drugs, 229
 to vaccines, 229
 Hyperthyroidism, 741
 Hypertrichosis, 573
 Hypertrophy, 538
 of heart, 584
 Hypochlorhydria, 653
 Hypodermic needles, sterilization
 of, 158
 syringes, sterilization of, 158
 Hypophysis, diseases of, 742
 Hypopituitarism, 745
 Hypostases, postmortem, 478
 Hypostatic congestion, 481
 Hypothyroidism, 738
 Hypotrichosis, 573

I

Icterus, 469, 679
 Ichthyosis, 573
 Idiosyncrasies to drugs, 229
 Illumination, dark-field, 98
 Immediate causes of disease, 456
 Immune agglutinins, 195
 bodies, 191, 192
 classification of, 191
 serum, 212
 injection followed by anaphylaxis, 227
 kinds of immunity produced
 by, 212
 serums often confused with vaccines, 212
 Immunity, 189
 acquired, 202
 active, 203
 and colony type, 76
 classified, 202
 due to antibody formation, 191
 Ehrlich's theory, 192
 examples of, 189
 in diphtheria, 291
 in erysipelas, 322
 in pneumonia, 308
 in scarlet fever, 319
 in smallpox, 367
 in staphylococcus infections, 325
 in streptococcus infections, 317
 in syphilis, 395
 in tetanus, 299
 in tuberculosis, 275
 in typhoid fever, 259
 in whooping cough, 344
 natural, 202
 passive, 203
 placental transfer, 203

Immunity—Cont'd
 produced by vaccines, 203, 212
 producing diseases, 190
 racial, 202
 relation to exposure to disease,
 204
 species, 202
 theories of, 190
 origin of, 34
 to hemophilus pertussis, 344
 Immunological methods of diagnosing disease, 205
 of studying bacteria, 205
 Importance of bacteria, 66
 of knowledge of pathology, 440
 Inclusion bodies, 364
 Incompetency of heart valves, 589
 Incubation period, 184, 503
 Incubator, bacteriological, description of, 54
 Index, opsonocytophagic, 201
 Indican in urine, 704
 Indirect cell division, 62
 contact, diseases spread by, 233
 Industrial bacteriology, 171
 Infantile paralysis, 375
 scurvy, 534
 Infants, diarrheas of, 266
 immunity in, 203
 summer diarrheas of, 266
 Infarct, 474
 Infarction, 474
 Infection, 179
 defense of body against, 189
 droplet, 233
 endogenous, 180
 exogenous, 180
 factors influencing, 182
 focal, 185
 food, 252
 fusospirillary, 398
 general, 185
 pathological changes in, 504
 local, 185
 mixed, 185
 mode of reaching body, 180
 occurrence of, factors influencing, 182
 Plenciz theory, 30
 primary, 185
 reservoir of, 237
 secondary, 185
 source of bacteria, causing, 179
 terminal, 186
 types produced by bacteria, 185
 Infections spread by air, 233
 by flies, 234
 Infectious diseases, 503
 disinfection in, 164

- Infectious**—Cont'd
 hepatitis, 382, 677
 mononucleosis, 606
- Infiltration**, amyloid, 468
 calcium, 468
 cholesterol, 469
 glycogen, 469
 uratic, 469
- Infiltrations**, 467
- Inflammation**, 490
 adhesions in, 499
 cause of disturbed functions in, 493
 of heat in, 493
 of pain in, 493
 of swelling in, 493
 causes of, 490
 chronic, 491, 499
 contraction of scars in, 499
 fever in, 498
 granulomatous, 500
 leucocytosis in, 498
 local changes in, 491
 purpose of, 490
 repair of, 493
 resolution in, 493
 signs of, 492
 suppuration in, 493
- Inflammatory exudate**, 490
- Influenza**, 341, 372
 bacilli (*see* Hemophilus influenzae)
 epidemiology of, 373
 swine, 374
 vaccine, 219
 virus of, 373
- Inguinal hernia**, 656
- Inherited diseases**, 455
- Inoculation of animals**, 121
 to prevent disease, 433
- Insects as conveyers of disease**, 179
 biological transfer of disease by, 234
 mechanical transfer of disease by, 234
- Instruments**, sterilization of, 158
- Insufficiency of heart valves**, 589
- Insulin**, 747
- Interdependence of organs**, 451
- Intermediate host**, 662
- Intermittent fever**, 464
 sterilization, 140
- Intestine**, cancer, 660
 diseases of, 654
 diverticula, 654
 intussusception, 659
 rupture, 657
 strangulation, 657
- Intestine**—Cont'd
 tuberculosis of, 518
 volvulus, 659
- Intestinal bacteria**, 667
 carriers, 236
 ciliates, 430
 concretions, 471
 flagellates, 430
 flora, normal, 255
 obstruction, 657
 chronic, 659
 paralytic, 658
 protozoa, 660
 worms, 662
- Intravenous medication**, preparation of rubber tubing for, 160
- Intrinsic factors** producing tumors, 541
- Intussusception**, 659
- Involution forms**, 75
- Iodine as disinfectant**, 152
- Irritation**, relation to tumors, 542
- Ischemia**, 482
- Ischiorectal abscess**, 672
- J**
- Jaundice**, 679
 homologous serum, 382, 681
- Jenner**, Edward, 31
- Joints**, acute arthritis, 755
 chronic arthritis, 756
 diseases of, 749, 755
 gonorrheal arthritis, 757
 osteoarthritis, 757
 syphilis of, 760
 tuberculosis of, 758
- K**
- Kala-azar**, 427
- Keloid**, 550
- Kidney disease**, edema of, 484
 uremia in, 693
 diseases of, 691
 hemorrhage from, 691
 nephritis, 691
 pelvis, diseases of, 695
 stones, 470, 696
 tuberculosis of, 693
 tumors of, 694
- Kinds of antibodies**, 192
 of immunity, 202
- Kircher**, athanasius, 29
- Koch**, Robert, 33
- Koch's laws** (or postulates), 33, 186
- Koch-Weeks bacillus**, 346

L

Labeling serums and vaccines, 219
 Laboratory diagnosis of gonorrhea, 331
 of leprosy, 282
 of pneumonia, 308
 of syphilis, 396
 of tuberculosis, 277
 of typhoid fever, blood cultures in, 259
 exercises, 762
 rules, 762
 Lactobacillus acidophilus, 175, 225
 bifidus, 255
 Lacunar tonsillitis, 645
 Laryngitis, 616
 Larynx, 616
 Laws of Koch, 33, 186
 Laveran, 34
 Lead line, 470
 Leeuwenhoek, father of bacteriology, 29
 Leprosy, 281, 518
 laboratory diagnosis of, 282
 pathology, 519
 prevention, 282
 Lesions of disease, 451
 Leucemia, 605
 lymphocytic, 605
 myeloid, 605
 Leucodins, 92
 Leucocytes, 602
 classification of, 602
 decreased, 603
 differential count, 602
 in bronchopneumonia, 509
 in epidemic meningitis, 509
 in pneumonia, 506
 in various diseases, 603
 increased, 603
 normal number, 602
 Leucocytosis, 184, 603
 caused by bacteria, 184
 in inflammation, 498
 polymorphonuclear, 603
 Leucoderma, 572
 Leucopenia, 603
 Ligatures, sterilization of, 160
 Light effects on bacteria, 82
 production by bacteria, 93
 Lime as disinfectant, 150
 chlorinated, 151
 Linens, sterilization of, 159
 Lip, cancer of, 643
 chancere of, 642
 diseases of, 641
 early recognition of cancer, 564
 syphilis of, 642
 Lipomas, 550

Lister, Joseph, 34
 Lithopedion, 717
 Liver, abscess of, 677
 acute yellow atrophy of, 676
 cirrhosis of, 678
 diseases of, 676
 fatty metamorphosis, 676
 infectious hepatitis, 677
 portal obstruction, 676
 spots, 572
 tumors of, 679
 Living conditions as cause of disease, 459
 Livores, 478
 Lobar pneumonia, 305, 505
 complications of, 506
 leucocytes in, 506
 stages of, 506
 Local anemia, 482
 effects of bacteria, 184
 infection, 185
 Localization, elective, 183
 Localized inflammation, 491
 Lock jaw, 296
 Locomotion of unicellular organisms, 63
 Locomotor ataxia, 635
 Lower animals, streptococcus infections of, 316
 forms of animal life, 44
 Lumpy jaw in cattle, 410
 Lung, abscess, 618
 and stomach, differentiation of hemorrhage from, 647
 stones, 472
 Lungs, atelectasis of, 618
 circulatory disturbances, 617
 emphysema, 617
 hemorrhage from, 617
 tuberculosis of, 515
 tumors of, 618
 Lymph node deposit in disease, 462
 nodes, enlargement, 609
 Hodgkin's disease, 611
 syphilis of, 611
 tuberculosis of, 610
 tumors of, 612
 Lymphadenitis, 610
 Lymphangiomas, 552
 Lymphatic leucemia, 605
 Lymphocytosis, 603
 Lymphogranuloma, venereal, 382
 Lymphomas, 562
 Lysis, 504

M

Magnifying glass, 29
 Making cultures, 112

- Malaria**, 419, 524
 cause of symptoms, 421
 development of parasite in mosquito, 421
 immunity in, 423
 laboratory diagnosis, 423
 mode of infection, 420
 mosquitoes transmitting, 423
 parasite, 420
 development in man, 420, 421
 discovery, 34
 of mode of transmission, 34
 pathology of, 524
 prevention, 425
 types of, 420
Male organs of reproduction, diseases of, 731
Malformations, 571
Malignancy of tumors, estimating, 562
Malignant pustule, 348
 tumors, 554
 connective tissue, 559
 epithelial, 556
 radiation therapy, 566
Malt, 175
Malta fever (*see* Brucellosis)
Mammary glands (*see* Breast)
 diseases of, 725
 fibroadenoma, 726
 mastitis, 725
Manifestations of disease, 451
Mantoux test, 278
Manufacture of alcoholic beverages, 175
 of dairy products, 174
 of serums, 213
 of vaccines, 216
 of vinegar, 176
Mastigophora, 419
Mastitis, 725
Mathematics of microscope, 48
Mattresses, disinfection of, 166
Maximum temperature for bacterial growth, 80
Measles, 369
 complications of, 371
 gamma globulin in, 370
 immune globulin in, 370
 immunity, 370
 leucocyte count in, 603
 mode of transmission, 370
 prevention, 371
 secondary infection in, 371
Measuring cells, 59
Mechanical means of destroying bacteria, 135
 transfer of disease by insects, 234
Meckel's diverticulum, 654
Media most suited for growing bacteria, 111
Medium, reaction of, effect on growth of bacteria, 82, 109
Melanomas, 550, 561
Membrane, cell, 60
Meninges, 624
 inflammation, 624
 hemorrhage, 624
Meningitis, 334
 cerebrospinal epidemic, 334
 epidemic (*see also* Meningococci), 509
 purulent, 624
 tuberculous, 625
Meningococci, action of sulfonamide compounds on, 154
 compared with gonococci, 335
 immunity produced by, 337
 laboratory diagnosis of infection, 337
 mode of infection, 336
 pathogenicity, 336
 source of infection, 336
 specific therapy, 338
 toxin of, 335
 types, 335
Meningococcus carriers, cultures for detection, 131
 detection, 338
 characteristics of, 334
 infections, prevention of, 338
Menorrhagia, 717
Menstruation, precocious, 718
 vicarious, 718
Mercresin, disinfectant action of, 148
Mercuric iodide as disinfectant, 148
Mercurochrome as disinfectant, 148
Mercury bichloride as disinfectant, 147
Merthiolate as disinfectant, 148
Metachromatic granules, 70
Metamorphosis, fatty, 647
Metaphen, antiseptic action of, 148
Metastasis of tumor cells, 554
Methods of examining tissues, 442
 of studying bacteria, 96
Metrorrhagia, 717
Micro-aerophiles, 82
Microbes, relations to other things, 42
Microbial diseases, treatment with chemicals, 153

- Microbiologist, equipment of, 46
 Microbiology, branches of, 42
 history of, 29
 principles of, 29
 recent advances in, 39
 relation to other sciences, 42
 value, 29
 of knowledge of, 39
 Microcephalia, 578
 Micrococci, 68
 Micrococcus catarrhalis, 339
 tetrangenus, 325
 Micron, 59
 Microscope, care and use of, 46
 description of, 46
 electron, 52
 manufacturers, early American, 38
 mathematics of, 48
 Miliary tuberculosis, 513
 Military personnel preventive inoculation, 436
 Milk, 246
 bacteria in, 246
 certified, 250
 diseases transmitted by, 247
 grading, 249
 in spread of typhoid fever, 258
 of lime, 150
 pasteurized, 248
 raw versus pasteurized, 251
 supply safe, requirements, 251
 Milk-borne epidemics, 247
 Minimum lethal dose, 213
 temperature of bacterial growth, 80
 Misplaced tissue, 580
 Mitosis, 62
 Mixed cultures, 107
 infection, 185
 vaccines, 216
 Moist gangrene, 474, 475
 heat sterilization, 137
 Moisture requirement of bacteria, 80
 Molds, 402
 classification of, 404
 description of, 402
 diseases caused by, 407
 growth of, 403
 importance of, 404
 plant diseases caused by, 414
 reproduction, 403
 Moles, pigmented, 552, 573
 Mongolism, 579
 Monilia infections, 413
 Monsters, 571, 580
 Morax-Axenfeld bacillus, 346
 Mordants, 100
 Mosquito, development of malaria parasite in, 421
 Mosquitoes, transmitting malaria, 423
 Motility of bacteria, 70
 of protozoa, 418
 Motion, ameboid, 63
 Brownian, 71
 Mouth and nose, bacteria leaving body by, 186
 diseases of, 641
 disinfection of discharges, 167
 early recognition of cancer, 564
 syphilis of, 642
 tumors of, 643
 Mucoid degeneration, 467
 Mucous membranes, disinfection of, 164
 patches, 642
 Multilocular cystadenomas, 549
 of ovary, 712
 Mumps, 372
 Murmurs, 587
 Muscle tumors, benign, 553
 Mycelia, 402
 Mycobacteria, 73
 Mycobacterium leprae, 281
 smegmatis, 282
 tuberculosis, characteristics of
 bovine type, 272
 collecting sputum for examinations, 130
 cultural characteristics, 270
 discovery of, 33
 distribution of, 269
 effects on body, 275
 general characteristics, 270
 immunity to, 275
 importance, 269
 kinds, 271
 mode of exit from body, 274
 of infection, 273
 source of infection, 273
 spread in body, 513
 toxic products, 272
 Mycology, 402
 Mycosis, 402
 Myeloid leucemia, 605
 Myomas, 553
 Myopia, 574
 Myxedema, 738
 Myxoma peritonei, 688

 N
 Nabothian cysts, 719
 Names, biological, 43
 Nasal discharges, disinfection of, 167
 polyps, 615

Natural immunity, 202
 methods of destroying bacteria,
 142
 Nature, bacteria in processes, 172
 of disease, 450
 Near-sightedness, 574
 Necator americanus, 665
 Neck, cysts and fistulas, 575
 Necrobiosis, 473
 Necrosis, 473
 caseation, 515
 causes of, 473
 fat, 685
 ischemic, 474
 Needles, hypodermic, sterilization
 of, 158
 Negative chemotaxis, 83
 Negri bodies, 379
 Neisseria gonorrhea (*see* Gono-
 cocci)
 Neosilvol as disinfectant, 149
 Nephritis, 691
 symptoms of, 692
 uremia in, 693
 urine in, 708
 Nephrolithiasis, 696
 Nephrosis, 691
 Nervous system, diseases of, 624
 syphilis of (*see* Neurosyph-
 ilis)
 Neurosyphilis, 523, 633, 635
 cerebrospinal fluid in, 638
 Nevi, pigmented, 549
 vascular, 572
 Newborn, care of eyes, 333
 Nipple, discharges from, 726
 Paget's disease of, 729
 Nitric acid as disinfectant, 149
 Nitrifying bacteria, 174
 Nitrogen cycle, 173
 fixation, 174
 Nonepidemic encephalitis, 631
 meningitis, 624
 Nonpathogenic bacteria, 66
 Nonspecific agglutinins, 196
 Normal cells and tumor cells com-
 pared, 543
 Nose and mouth, bacteria leaving
 body by, 186
 cultures, collecting, 131
 diseases of, 615
 disinfection of discharges, 167
 rhinitis, 615
 Nuclear membrane, 60
 Nucleolus, 61
 Nucleus of cell, 61
 function of, 61
 Nutrition of unicellular organ-
 isms, 63
 as a cause of disease, 454

O

O-agglutinins in typhoid fever,
 260
 Obligate aerobes, 82
 Obstructed appendix, 671
 hernia, 656
 Obstruction, appendicular, 671
 intestinal, 657
 Obstructive jaundice, 680
 Occupation as cause of disease,
 455
 Occurrence of infection, factors
 influencing, 182
 Odors, production by bacteria, 93
 Old tuberculin, 272
 -oma, meaning of, 544
 Operating room, disinfection of,
 163
 Operation, field of, disinfection
 of, 163
 of autoclave, 140
 Ophthalmia neonatorum, preven-
 tion, 149, 333
 Opsonins, 199
 Opsonocytaphagic index, 201
 Optimum temperature of bacterial
 growth, 80
 Oral cancer, 643
 carriers, 236
 cavity, diseases of, 642
 Orchitis, 731
 Organisms, drug-fast, 77
 unicellular, 59
 Organs, interdependence of, 451
 susceptibility to cancer, 558
 vital, 476
 Osmosis, effects on bacteria, 83
 Osteitis, 749
 Osteomas, 552, 753
 Osteomyelitis, 749
 Ovary, carcinoma of, 713
 cystadenomas of, 710
 cysts of, 710
 dermoid, 713
 diseases of, 710
 Oxygen requirements of bacteria,
 82
 Oxyuris vermicularis, 666

P
 P.P.D., 272
 Paget's disease of nipple, 729
 Palate, cleft, 575
 Pancreas, diseases of, 685, 747
 fat necrosis, 685
 relation to diabetes mellitus,
 747
 Pancreatitis, 686
 Pandemic disease, 186

- Papillary cystadenomas, 549, 712
 Papillomas, 547
 Paralysis, infantile, 375
 Paralytic obstruction of intestine, 658
 Parasites, 79
 facultative, 79
 strict, 79
 Parathyroid glands, diseases of, 742
 Paratyphoid bacilli, 263
 Paresis, general, 633
 Parotitis, epidemic, 372
 Parts of bacteria, stains for, 105
 Passive anaphylaxis, 223
 carriers, 236
 hyperemia, 480
 immunity, 203
 in infants, 203
 therapeutic application, 203
 Pasteur, Louis, 32
 studies on spontaneous generation, 32
 treatment for rabies, 217
 discovery of, 33
 Pasteurella pestis, 352
 tularensis, 354
 Pasteurization, 82, 142
 Pasteurized milk, 248
 versus raw milk, 251
 Patch test for tuberculosis, 278
 Pathogenesis of disease, 452
 Pathogenic bacteria, 66
 mode of reaching body, 180
 spore-forming, 72
 Pathogenicity of staphylococci, 324
 Pathologist, autopsy, 448
 clinical, 441
 surgical, 442
 Pathology, clinical, 441
 definition, 439
 departments in hospitals, 441
 divisions, 439
 importance, 440
 relation to other sciences, 439
 value of, 440
 Pellagra, 531
 Penicillin, 155
 collection of blood for estimating, 130
 discovery of, 35
 inhibiting culture media, 111
 sensitivity to, 229
 Penicillinase, 112
 Peptic ulcer, 647
 Perforation in typhoid fever, 511
 Period of incubation, 184, 503
 Periostitis, 749
 Peritoneal fluid, collecting for bacteriological examinations, 133
 Peritoneum, disease, 686
 pseudomyxoma peritonei, 688
 tumors of, 688
 Peritonitis, 686
 tuberculous, 688
 Permit to perform autopsy, 449
 Pernicious anemia, 599
 Pertussis bacillus (*see* Hemophilus pertussis)
 Petechiae, 483
 Petri dish, description of, 113
 Phagedena, 498
 Phagocytic cells, 200
 theory of immunity, 190
 Phagocytosis, 200
 important cells, 200
 Pharyngitis, 644
 Phenol as disinfectant, 152
 coefficient, 146
 Phlegmon, 498
 Phthisis, fibroid, 518
 Physical means of sterilization, 136
 Pigment production of bacteria, 93
 Pigmentation, 469
 Pigmented nevi, 549
 Pilonidal cyst and sinus, 579
 Pink eye, 346
 Pinworms, 666
 Pituitary body, diseases of, 742
 cachexia, 745
 Placenta, bacteria entering body by, 181
 Plague, 351
 clinical types, 352
 mode of infection, 352
 Plant diseases caused by molds, 414
 Plants, difference from animals, 42
 Plasmodium falciparum, 420, 421
 malariae, 420, 421
 vivax, 420, 421
 Plasmolysis, 84
 Plasmoptysis, 83
 Platelets, blood, 606
 Plates, 114
 streak, 117
 Plating, 114
 counting bacteria by, 118
 Platinum loop, description of, 97
 Plenciz, theory of infection, 30
 Pleomorphism, 75
 Pleura, diseases of, 621
 Pleural fluid, collecting, 133

- Pleurisy, tuberculous, 518
 Pleuritis, 621
 Pneumococci, action of sulfonamide compound on, 154
 characteristics of, 305
 determination of types, 308
 differentiation from streptococci, 309
 diseases caused by, 311
 toxin production of, 307
 types of, 306
 Pneumococcus, 305
 carriers, 308
 pathogenicity, 307
 Pneumonia, 305, 505
 alba, 524
 epidemiology of, 307
 immunity in, 307, 308
 kinds, 305
 laboratory diagnosis of, 308
 lobar, causes other than pneumococci, 311
 mode of infection, 307
 prevention, 311
 specific therapy, 311
 virus, 383
 Pneumoconiosis, 470
 Pneumoliths, 472
 Pneumothorax, 621
 Pointing of abscess, 498
 Poisoning, food, 252
 Polar bodies, 70
 in *C. diphtheriae*, 286
 Poliomyelitis, 375
 cerebrospinal fluid in, 638
 epidemiology, 375
 immunity in, 376
 types of, 375
 Pollution of water, 240, 241
 Polyavitaminosis, 527
 Polydactylism, 577
 Polyps of uterus, 721
 Polyvalent serum, 215
 vaccine, 216
 Pork tapeworm, 665
 Port wine stains, 533, 573
 Portal obstruction, 676
 Positive chemotaxis, 83
 Postmortem (*see* Autopsy), 448
 hypostases, 478
 Postulates of Koch, 33, 186
 Potassium permanganate as disinfectant, 150
 Pott's disease, 750
 Precipitins, 198
 Precocious menstruation, 718
 Predisposing causes of disease, 452
 Pregnancy, abdominal, 716
 anemia of, 600
 ectopic, 716
 extrauterine, 716
 tests for, 742
 Prenatal syphilis, 390, 395, 522
 Preparation of antitoxins, 213
 of vaccines, 216
 Preservation, 144
 Preserving food, 253
 origin of, 32
 Pressure, effect on bacteria, 84
 Preventive inoculation in diphtheria, 433, 434
 in military personnel, 436
 in rabies, 433, 436
 in scarlet fever, 434, 435
 in smallpox, 434, 435
 in tetanus, 434, 436
 in typhoid fever, 434, 436
 in whooping cough, 433, 435
 Prevention of botulism, 303
 of diphtheria, 294
 of epidemic meningitis, 338
 of leprosy, 282
 of pneumonia, 311
 of scarlet fever, 320
 of streptococcus infections, 317
 of syphilis, 397
 of tetanus, 299
 of tuberculosis, 279
 of typhoid fever, 260
 Primary anemias, 597, 599
 infections, 185
 takes, 368
 union, 496
 Principles of biological classification, 43
 of complement fixation, 205
 of microbiology, 29
 Products of growth, effects on bacteria, 83
 Progressive tissue changes, 466
 Prolapse of rectum, 675
 Prostate gland, carcinoma, 735
 metastasis to bone, 755
 diseases of, 733
 enlargement of, 734
 tuberculosis of, 734
 Prostatic concretions, 471
 hyperplasia, 434
 Prostatitis, 733
 Protargol as disinfectant, 149
 Proteolytic enzymes, 88
 Proteus bacilli, 360
 relation to Weil-Felix reaction, 361
 Protoplasm, 59
 Protozoa, 416
 characteristics of, 416

- Protozoa—Cont'd
 classification of, 419
 cyst formation, 418
 diseases caused by, 419
 motility, 418
 nutrition of, 416
 reproduction, 419
 structure of, 416
 Provocative dose in allergy, 222
 Pseudomembranous exudate, 491
 Pseudomonas pyocyanea, 360
 Pseudomucinous cystadenomas,
 549, 712
 Pseudomyxoma peritonei, 688
 Psilosis, 413
 Psoas abscess, 752
 Ptomaines, 89
 Puerperal sepsis, 322
 Pulmonary tuberculosis, 515
 Pulse rate and body temperature,
 464
 Pure cultures, 107, 113
 methods of studying, 118
 obtaining, 114
 Purification of water, 242
 Purulent exudate, 491
 meningitis, 624
 cerebrospinal fluid in, 637
 Pus, 494
 from abscesses, collecting, 132
 for bacteriological examina-
 tions, collecting, 132
 in urine, 706
 tube, 715
 Putrefaction, 88
 Pyelitis, 695
 Pyemia, 185
 Pylorus, congenital hypertrophic
 stenosis, 646
 Pyogenic cocci, 305
 Pyonephrosis, 696
 Pyosalpinx, 715
 Pyuria, 706
- Q**
- Qualities of good disinfectants,
 145
 Quartan malaria, 420
- R**
- Rabbit fever (*see* Tularemia)
 Rabbits as source of tularemia,
 355
 Rabies, 378
 handling suspected animals, 379
 incubation, 379
 Pasteur treatment, discovery of,
 33
 preventive inoculation, 433, 436
 Rabies—Cont'd
 transmission of, 379
 vaccine, preparation of, 217
 Race as cause of disease, 454
 Races, incidence of tuberculosis
 in, 276
 Rachitis, 529
 Racial immunity, 202
 Radiation of malignant tumors,
 566
 Radium as cause of disease, 458
 effects on bacteria, 83
 Rat-bite fever, 398
 Raw and pasteurized milk, com-
 pared, 251
 Ray fungus, 410
 Reaction of culture media, 109
 of immunity, 368
 of medium, effects on bacteria,
 82
 of tissue to foreign bodies, 500
 Reasons for animal inoculation,
 122
 Recent advances in microbiology,
 39
 Rectal fistula, 673
 strictures, 675
 Rectum, cancer of, 675
 diseases of, 672
 hemorrhoids, 674
 prolapse, 675
 Red blood cells, 596
 degeneration, 721
 Reducible hernia, 656
 Reductases, 88
 Regeneration, 500
 kinds, 500
 of tissues, 501
 Regressive tissue changes, 466
 Regurgitation of heart valves, 589
 Relapsing fever, 397
 Relation of bacteria to disease,
 179
 of cowpox and smallpox, 31
 of microbes to other things, 42
 of microbiology to other sci-
 ences, 42
 Remittent fever, 464
 Renal calculi, 470, 696
 hemorrhage, 691
 Repair of wounds, 494
 Reproduction of bacteria, 71
 of molds, 403
 of protozoa, 419
 of unicellular organisms, 64
 Requirements for bacterial growth,
 79
 for safe milk supply, 251
 Reservoir of infection, 237

Resolution, 493
 Respiration of unicellular organisms, 63
 Respiratory tract, bacteria entering body by, 181
 leaving body by, 186
 Response to stimuli of unicellular organisms, 63
 Results of hemorrhage, 483
 Retropharyngeal abscess, 644
 Retting of flax and hemp, 177
 Rh factor, 601
 Rhagades, 523
 Rheumatic fever, 505
 Rhinitis, 615
 Rhinoliths, 471
 Rickets, 529
 Rickettsiae, 388
 Rigor mortis, 477
 Ringworm, 408
 Rocky Mountain spotted fever, 389
 vaccine, 219
 Rodent ulcer, 559
 Rooms, fumigation of, 168
 Roundworms, 666
 R-type colonies, 75
 Rubber goods, sterilization of, 160
 tubing, preparation for intravenous use, 160
 Rubeola (*see* Measles)
 Rules for collection of specimens, 126
 Rupture of intestine, 657

S

Sabre tibia, 523
 Safe milk supply, requirements, 251
 Salmonella, 263
 Salpingitis, 714
 leucocyte count in, 603
 tuberculous, 716
 Salt solution, sterilization of, 160
 Sanitation of swimming pools, 244
 Sappremia, 185
 Saprophytes, 79
 facultative, 79
 strict, 79
 Sarcodina, 419
 Sarcoma, giant cell (*see* Epulis and Giant cell tumor)
 meaning, 545
 metastasis, 554, 561
 Sarcomas, 554, 559
 Sauerkraut, 176
 Scarletina, 504
 Scarlet fever, 504
 antitoxin, 320

Scarlet fever—Cont'd
 Dick test in, 319
 immunity in, 319
 mode of infection, 318
 prevention, 320
 preventive inoculation, 434, 435
 Schultz-Charlton phenomenon, 320
 source of infection, 318
 specific therapy of, 320
 streptococci, 318
 toxin of, 318
 toxin, 219
 Sears, contraction of, 499
 Schick test, 292
 Schultz-Charlton, phenomenon, 320
 Sciences related to pathology, 439
 Scrofula, 611
 Scrubbing, 135
 Scurvy, 533
 Seatworms, 666
 Secondary abdominal pregnancy, 717
 anemia, 597, 598
 infection, 185
 union, 496
 Sedimentation, 136
 Selective culture media, 110
 Self-limited diseases, 504
 Senile gangrene, 476
 Sensitivity to penicillin, 229
 to sulfonamide drugs, 229
 Sensitizing dose in allergy, 222
 Sepsis, puerperal, 322
 Septic sore throat, 322
 Septicemia, 185
 Serous cystadenomas, 549
 of ovary, 712
 exudate, 490
 Serum, antibacterial, 215
 convalescent, 215
 immune, 212
 kind of immunity produced by, 212
 often confused with vaccines, 212
 sickness, 227
 Serums and vaccines compared, 212
 dating, 219
 manufacture of, 219
 Sewage, 244
 Sex as cause of disease, 453
 Shaking, effect on bacteria, 84
 Shape of bacteria, 67
 of cells, 59
 Shoes, disinfection of, 166
 Sick-cell anemia, 601

- Sickness, serum, 227
 Side-chain theory of immunity, 192
 Signs of death, 476
 of disease, 451
 of inflammation, 492
 Silicosis, 470
 Silver nitrate as disinfectant, 149
 in eyes of newborn, 149
 Sinus, 498
 Site of operation, disinfecting, 163
 Situs inversus, 577
 Size, abnormalities of, 571
 of bacteria, 68
 of cells, 59
 Skin, abnormalities of, 571
 bacteria entering body by, 181
 early recognition of cancer, 564
 eruptions, allergic, 229
 fungus diseases of, 407
 test dose, 214
 Slaked lime, 150
 Sleeping sickness, 377, 425
 Slide, hanging drop, 97
 Smallpox, 365
 and cowpox, relation, 31, 367
 immunity in, 367
 leucocyte count in, 603
 preventive inoculation, 434, 435
 transmission of, 366
 types of virus, 365
 vaccination, 367
 discovery of, 31
 vaccine, 217, 367
 Smear, definition of, 99
 Smears for gonococci, collecting, 132
 Smegma bacillus, 282
 Smoking, food, 253
 Snake antivenin, 214
 Snuffles, 523
 Soap, antiseptic action of, 147
 Softening of brain, 630
 Soiled clothing, disinfection of, 165
 Somatic death, 471
 Sore throat, septic, 322
 Source of bacteria causing infection, 179
 Sources of communicable diseases, 180
 of water, 240
 Special activities of bacteria, 87
 Species, 43
 immunity, 202
 Specific organisms, stains for, 105
 therapy of diphtheria, 293
 Specimens, collection of, 126
 Spider antivenins, 214
 Spina bifida, 579
 Spine, tuberculosis of, 750
 Spirilla, 73
 Spirillum, definition of, 67
 Spirochete, definition of, 67
 Spirochetes, 73, 392
 Spleen, 613
 Splenic fever, 348
 Spontaneous generation, theory of, 31
 Sporadic disease, 186
 Spore formation, 72
 Spores, 71
 characteristics of, 72
 of fungi, 403
 effects of heat on, 82
 staining of, 72
 Sporotrichosis, 411
 Sporozoa, 419
 Sporulating bacteria, 72
 Spotted fever, 333
 Spreading factor, 93, 315
 Sprue, 413
 Sputum, 619
 collecting for examinations, 130
 disinfection of, 167
 general characteristics, 619
 in disease, 620
 Stages of syphilis, 394
 Stain, acid-fast, 103
 Gram's, 101
 Staining bacteria, 99
 methods, origin of, 33
 of spores, 72
 Stains, classes of, 100
 differential, 101
 for parts of bacteria, 105
 for specific organisms, 105
 general, 100
 Standardizing disinfectants, 146
 Standards for drinking water, 242
 Staphylococci, 68, 323
 action of sulfonamide compounds on, 154
 characteristics of, 323
 classification of, 323
 diseases caused by, 324
 mode of infection, 324
 pathogenicity of, 324
 sources of infection, 324
 Staphylococcus albus, 323
 aureus, 323
 citreus, 323
 food intoxication, 253
 infections, bacteriological diagnosis, 325
 immunity in, 325
 specific therapy, 325
 toxic products of, 324

- Status lymphaticus, 746
 Steam sterilization, 139
 under pressure, sterilizing by, 140
 Stenosis of esophagus, 646
 Sterilization by dry heat, 141
 by heat, 137
 by physical means, 136
 by steam, 139
 under pressure, 140
 by sunlight, 142
 fractional, 140
 intermittent, 140
 of catheters, 160
 of cystoscopes, 161
 of dressings, 159
 of gloves, 159
 of hand brushes, 160
 of hypodermic needles, 158
 syringes, 158
 of instruments, 158
 of ligatures, 160
 of linens, 159
 of rubber goods, 160
 of salt solution, 160
 of sutures, 160
 of vaccines, 138
 of water, 160
 surgical, 158
 Stock vaccines, 216
 Stomach and lungs, differentiation of hemorrhage, 647
 blood in, 654
 cancer of, 650
 congenital defects, 646
 contents in cancer of, 654
 in ulcer of, 654
 methods of examining, 651
 diseases of, 646
 hemorrhage of, 647
 ulcer of, 648
 Stomatitis, 641
 Stones, bladder, 699
 Strangulated hernia, 656
 Strangulation of intestine, 657
 Strawberry marks, 553
 Streak plates, 117
 Streptobacilli, 68
 Streptococci, 68, 312
 action of sulfonamide compounds on, 154
 as causes of disease in lower animals, 316
 causing scarlet fever, 318
 characteristics of, 312
 classification of, 313
 differentiation from pneumococci, 309
 human diseases caused by, 315, 504
 Streptococci—Cont'd
 Lancefield's classification, 314
 mode of infection, 316
 pathogenicity of, 315
 poisons produced by, 315
 source of infection, 316
 Streptococcus hemolyticus, 314
 immunity, 317
 infections, 317
 laboratory diagnosis, 317
 prevention of, 317
 specific therapy, 317
 viridans, 214, 316
 Streptomycin, 155
 discovery of, 35
 Strict parasites, 79
 Stricture of esophagus, 646
 of rectum, 675
 of urethra, 701
 Strongyloides intestinalis, 666
 Structural changes, 451
 Structure of bacteria, 69
 of cells, 60
 Study of bacteria by animal inoculation, 107
 by cultural methods, 107
 Studying pure cultures, 118
 S-type colonies, 75
 Sugar in urine, 704
 Sulfonamide compounds, 155
 action on gonococci, 154
 on meningococci, 154
 on pneumococci, 154
 on staphylococci, 154
 discovery of, 35
 mode of action, 154
 sensitivity to, 229
 concretions, 472
 inhibiting culture media, 111
 Sulphur dioxide as disinfectant, 152
 Summer diarrheas of infants, 266
 Sunlight as sterilizing agent, 142
 Suppuration, 493
 Surgery, antiseptic, origin of, 34
 Surgical disinfection and sterilization, 158
 pathology, 442
 Sutures, sterilization of, 160
 Swelling, cloudy, 466
 Swimming pools, 244
 Swine influenza, 374
 Symbiosis, 84
 Symptoms of botulism, 303
 of disease, 451
 Syphilis, 392, 520
 congenital, 395, 522
 evolution of, 394
 immunity, 395
 laboratory diagnosis, 396

- Syphilis—Cont'd
 mode of infection, 393
 of bones, 752
 of joints, 760
 of lymph nodes, 611
 of mouth, 642
 of testis, 732
 prenatal, 395, 522
 prevention, 397
 relation to yaws, 397
 stages, 394, 520
 Syphilitic meningitis, 626
 Syringes, hypodermic, sterilization of, 158
- T
- Tabardillo, 388
 Tabes dorsalis, 635
 Taenia nana, 665
 saginata, 665
 solium, 665
 Tanning, 177
 Tapeworms, 662
 cycle of development, 663
 Teeth, Hutchinson's, 523
 Temperature and pulse rate, 464
 effects on bacteria, 80
 Teratomas, 566
 Terminal disinfection, 168
 infection, 186
 Tertian malaria, 420, 421
 Testis, diseases of, 731
 hydrocele, 732
 syphilis of, 732
 tuberculosis of, 731
 tumors of, 732
 Tests, agglutination, 196
 for hypersensitiveness, 230
 Tetanus, 520
 antitoxin, 213, 299
 clinical forms, 298
 immunity, 299
 mode of infection, 298
 prevention, 299
 preventive inoculation, 434, 436
 source of infection, 298
 toxoid, 218, 299
 Thallophytes, 44
 Theories of immunity, 190
 origin of, 34
 Therapeutic principles of active and passive immunity, 203
 Thermal death point, 137
 Thermogenesis, 463
 Thermolysis, 463
 Thermometers, disinfection of, 167
 Thermostat, principles of, 54
- Threadworms, 666
 Throat, bacteriological diagnosis of ulcerative lesions, 131
 cultures, collecting, 131
 diseases of, 644
 septic sore, 322
 Thrombi, canalization of, 487
 Thrombosis, 484
 cerebral, 630
 effects of, 486
 Thrombus, 484
 Thrush, 413
 Thymus gland, diseases of, 746
 Thyroid gland, carcinoma of, 741
 diseases of, 736
 physiology of, 736
 Tibia, sabre, 523
 Time of death, 478
 Tissue, method of examining, 442
 out of place, 580
 progressive changes, 538
 reaction to foreign body, 500
 regressive changes, 466
 Tobacco, curing, 177
 Tongue, cancer of, 643
 diseases of, 641
 Tongue-tie, 575
 Tonsillitis, 644
 Torula infections, 412
 Toxemia, 185
 Toxic products of mycobacterium tuberculosis, 272
 of staphylococcus, 324
 Toxin, antitoxin, 218, 291
 of Clostridium tetani, 297
 of Corynebacterium diphtheriae, 287
 of scarlet fever, streptococci, 219, 318
 production of pneumococci, 307
 Toxins, 90
 produced by meningococci, 335
 by pneumococci, 307
 Toxoid, alum-precipitated, 218
 diphtheria, 218, 292
 staphylococcus, 218
 tetanus, 218
 Toxoids, 92
 Transmission of communicable diseases, 233
 Transudates, 484
 Traumatism as cause of disease, 456
 Trench fever, 390
 mouth, 398
 Treponema pallidum, 392
 characteristics of, 392
 demonstration in lesions, 396

- Trichocephalus dispar, 667
 Trichomonas vaginitis, 724
 Tricresol as disinfectant, 152
 Trypanosomiasis, 425
 Tubal abortion, 717
 Tubercle bacilli (*see* Mycobacterium tuberculosis)
 Tubercles, 514
 Tuberculin, 272
 test, 278
 types of reaction to, 279
 Tuberculosis, 269, 512 (*see also* Mycobacterium tuberculosis)
 calcification in, 515
 disease, 275
 early symptoms, 278
 immunity in, 275
 incidence in different races, 276
 infection, 275
 laboratory diagnosis, 277
 leucocytes in, 603
 meaning of word, 513
 miliary, 513
 mode of infection, 273
 of bones, 750
 of Fallopian tubes, 716
 of intestine, 518
 of joints, 758
 of kidney, 693
 of lymph nodes, 610
 of prostate gland, 734
 of spine, 750
 of testis, 731
 origin of term, 513
 pathology, 514
 prevention of, 279
 pulmonary, 515
 signs of beginning disease, 278
 source of infection, 273
 specific therapy, 280
 spread within body, 513
 sputum in, 277
 tuberculin reaction in, 278
 Tuberculous arthritis, 758
 meningitis, 625
 cerebrospinal fluid in, 637
 peritonitis, 688
 pleurisy, 518
 salpingitis, 716
 Tubing, rubber, preparation for intravenous use, 160
 Tubo-ovarian abscess, 715
 Tularemia, 354
 clinical types, 355
 immunity, 356
 laboratory diagnosis, 356
 mode of infection, 355
 Tularemia—Cont'd
 prevention, 356
 specific therapy, 356
 Tumor, brain, 634
 cerebrospinal fluid in, 638
 capsule, 546
 cells and normal cells compared, 543
 resistance, 544
 giant cell, 561, 644
 Tumors, 541 (*see also* Cancer, Carcinoma, and Sarcoma)
 benign, 546
 connective tissue, 550
 epithelial, 547
 muscle, 553
 carcinogenic agents, 543
 classification, 544
 cause of death in, 566
 causes of, 541
 characteristics, 541
 economic importance, 563
 environmental control, 543
 estimating malignancy, 562
 functions of, 543
 heredity in, 541
 in children, 566
 malignant, 554
 by position, 546
 connective tissue, 559
 epithelial, 556
 metastasis of, 554
 mode of growth, 544
 nourishment of, 543
 of bones, 752
 of esophagus, 646
 of kidney, 694
 of liver, 679
 of lungs, 618
 of mouth, 643
 of nose, 615
 of peritoneum, 688
 of testis, 732
 radiation therapy, 566
 value of early diagnosis, 563
 Types, blood, 198
 of infection produced by bacteria, 185
 of malaria, 420
 of meningococci, 335
 of pneumococci, 306
 Typhoid bacillus (*see* Eberthella typhosa)
 fever, 510
 antibodies in, 258
 blood cultures in, 259
 carriers of, 258
 complications of, 511

- Typhoid fever—Cont'd
 feces cultures in, 259
 H-agglutinins, 260
 hemorrhage in, 511
 immunity in, 259
 laboratory diagnosis of, 259
 mode of spreading, 257
 O-agglutinins, 260
 perforation in, 511
 prevention of, 260
 preventive inoculation, 434, 436
 spread of, 257
 urine cultures in, 259
 vaccination in, 262
 vaccine first used, 34
 Widal test in, 259
 Typhus fever, 388
 endemic, 388
 epidemic, 388
 vaccine, 219, 389
 Tyrothricin, 155

U

- Ulcer, 498
 duodenal, 649
 of stomach, 648
 gastric contents in, 654
 rodent, 559
 Ulcerative lesion of throat, 290
 bacteriological diagnosis, 131
 stomatitis, 641
 Ultraviolet light, effects on bacteria, 82
 rays as a cause of disease, 458
 Umbilical hernia, 666
 Uncompensated heart lesions, 589
 Undulant fever (*see* Brucellosis)
 Unicellular organisms, 59
 circulation of, 63
 compared with multicellular organisms, 63
 excretion of, 63
 locomotion of, 63
 nutrition of, 63
 reproduction of, 64
 respiration of, 63
 response to stimuli, 63
 Union of wounds, 494
 Unit, antitoxin, 214
 Univalent serum, 215
 Unstained bacteria, examination of, 96
 Uratic infiltration, 469
 Uremia, 693
 Ureters, diseases of, 695
 Urethra, diseases of, 700
 stricture of, 701

- Urethral caruncle, 701
 Urethritis, gonorrheal, 700
 nonspecific, 700
 Urinary carriers, 236
 system, diseases of, 691
 Urine, 701
 abnormal constituents, 703
 albumin in, 704
 bacteria in, 706
 leaving body by, 186
 blood in, 706
 casts in, 705
 characteristics of, 701
 collection of, 128
 cultures in typhoid fever, 259
 disinfection of, 166
 in diabetes, 706
 in nephritis, 708
 normal composition, 703
 sugar in, 704
 Urticaria, 229
 U. S. Army preventive inoculations in, 436
 Navy preventive inoculations in, 436
 Use of bacterial vaccines, 216
 of microscope, 46
 Uterus, bicornate, 578
 cancer, 722
 chorionepithelioma, 724
 diseases of, 717
 early recognition of cancer, 565
 endocervicitis, 718
 endometritis, 718
 fibroids, 719
 fibromyomas, 719
 hemorrhage from, 717
 menorrhagia, 717
 metrorrhagia, 717
 polyps, 721

V

- Vaccination, smallpox, 367
 discovery of, 31
 typhoid fever, 262
 first used, 34
 yellow fever, 381
 Vaccine, B.C.G., 281
 definition of, 212
 influenza, 219
 polyvalent, 216
 rabies, 217
 Rocky Mountain spotted fever, 219
 smallpox, preparation of, 217
 typhus fever, 219, 389
 yellow fever, 219
 Vaccines, 212
 autogenous, 216

Vaccines—Cont'd

- bacterial, use of, 217
- dating and labeling, 219
- kind of immunity produced by, 212
- mixed, 216
- often confused with immune serums, 212
- preparation, 216
- sterilization of, 138
- stock, 216
- Vagina, disease of, 724
- Vaginitis, 724
- Value of knowledge of microbiology, 39
 - of microbiology, 29
 - of pathology, 440
- Valvular defects of heart, 588
- Variation of bacteria, 74
- Varicocele, 733
- Varicose veins, 593
- Variola (*see* Smallpox)
- Varix, 593
- Vascular nevi, 572
- Vegetations, heart, 587
- Vegetative bacteria, 72
- Veins, diseases of, 593
 - varicose, 593
- Veneral diseases, 328
 - lymphogranuloma, 382
- Vermiform appendix, 667
- Verruca vulgaris, 547
- Vesical calculi, 470, 699
- Vicarious menstruation, 718
- Vincent's angina, 398
- Vinegar, manufacture of, 176
- Virulence, 182
- Virus of influenza, types, 373
 - pneumonia, 383
- Viruses, classification, 364
 - disease caused by, 364
 - filtrable, 364
- Vital organs, 476
- Vitamin A, 528
 - B complex, 528
 - C, 528
 - D, 528
 - deficiencies, 527
 - K, 529
- Vitamins, 527
 - characteristics of, 527
 - naming, 527
- Vitiligo, 572
- Volvulus, 659
- Von Pirquet test, 278

W

- Warts, 547
- Wassermann test, 208
 - first used, 34
- Water, 239
 - bacteriological examination of, 240
 - bath, description of, 55
 - diseases spread by, 239
 - filtration, 243
 - purification of, 242
 - sources of, 240
 - sterilization of, 160
 - treatment with copper sulphate, 150
- Weil-Felix reaction, 361, 388
- Wet filter paper method of standardizing disinfectants, 146
- Whitewash, 150
- Whooping cough, 432
 - immunity, 344
 - prevention, 344
 - preventive inoculation, 433, 435
 - specific therapy, 344
- Widal test, 259
- Wine, diseases of, 32
- Women contributors to science of microbiology, 38
- Wool sorters disease, 348
- Work of useful bacteria, 171
- Worms, intestinal, 662
- Wounds, detrimental effects of
 - healing, 499
 - disinfection of, 164
 - repair of, 494

X

- X-ray as cause of disease, 458
 - effects on bacteria, 83

Y

- Yaws, relation to syphilis, 397
- Yeasts, 405
 - classification of, 406
 - economic importance of, 407
 - general characteristics of, 405
 - growth of, 407
 - reproduction of, 405
- Yellow fever, 380
 - vaccination, 381
 - vaccine, manufacture of, 219

**IMPERIAL AGRICULTURAL RESEARCH
INSTITUTE LIBRARY
NEW DELHI.**

Date of issue.	Date of issue.	Date of issue.
1.2.58		
21.5.58		
22.1.58		
18 JAN 1975		